

Inventor Search

SHAHNAN-SHAH 10/039,760

=> d his 11-16

(FILE 'HCAPLUS' ENTERED AT 09:50:50 ON 10 OCT 2003)

L1 223 S FINLAY B?/AU
L2 361 S POTTER A?/AU
L3 583 S L1-2
L4 41 S L3 AND VACCINE
L5 19 S L4 AND COLI
L6 4 S L5 AND ENTEROHEM?

=> d ibib abs ind 16 1-4

YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L6 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:966480 HCAPLUS
DOCUMENT NUMBER: 138:185831
TITLE: Current progress in enteropathogenic and enterohemorrhagic Escherichia coli vaccines
AUTHOR(S): Horne, Cathy; Vallance, Bruce A.; Deng, Wanyin; Finlay, B. Brett
CORPORATE SOURCE: Biotechnology Laboratory, University of British Columbia, Vancouver, BC, V6T 1Z3, Can.
SOURCE: Expert Review of Vaccines (2002), 1(4), 483-493
CODEN: ERVXAX; ISSN: 1476-0584
PUBLISHER: Future Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Enteropathogenic and enterohemorrhagic Escherichia coli are important causal agents of infectious diarrhea, particularly amongst pediatric populations. While enteropathogenic E. coli is a significant health threat in developing countries, enterohemorrhagic E. coli causes sporadic, sometimes deadly outbreaks of hemorrhagic colitis, with a serious complication, hemolytic uremic syndrome, occurring in a proportion of cases. This review discusses the pathogenesis of enterohemorrhagic and enteropathogenic E. coli, the host immune response and the current application of this knowledge towards efficacious vaccine strategies. Several lines of investigation indicate the feasibility of such strategies and justify further development of a vaccine targeting these significant intestinal pathogens.
CC 15-0 (Immunochemistry)
ST review Escherichia vaccine intimin diarrhea colitis
IT Diarrhea
Escherichia coli
Vaccines
(current progress in enteropathogenic and enterohemorrhagic Escherichia coli vaccines)
IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(current progress in enteropathogenic and enterohemorrhagic Escherichia coli vaccines)
IT Kidney, disease
(hemolytic-uremic syndrome; current progress in enteropathogenic and enterohemorrhagic Escherichia coli vaccines)
IT Intestine, disease
(hemorrhagic colitis; current progress in enteropathogenic and enterohemorrhagic Escherichia coli vaccines)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(intimins; current progress in enteropathogenic and enterohemorrhagic Escherichia coli vaccines)

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 4 HCPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2002:521530 HCPLUS
 DOCUMENT NUMBER: 137:92729
 TITLE: Vaccine compositions comprising enterohemorrhagic Escherichia coli antigen and immune adjuvant
 INVENTOR(S): Finlay, Brett; Potter, Andrew A.
 PATENT ASSIGNEE(S): University of Saskatchewan, Can.; University of British Columbia
 SOURCE: PCT Int. Appl., 53 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053181	A1	20020711	WO 2002-CA19	20020103
WO 2002053181	C1	20020919		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002160020	A1	20021031	US 2002-39760	20020103
EP 1349570	A1	20031008	EP 2002-726978	20020103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			US 2001-259818P	P 20010104
			WO 2002-CA19	W 20020103

AB Compns. and methods for stimulating an immune response against a secreted enterohemorrhagic Escherichia coli (EHEC) antigen are disclosed. The compns. comprise EHEC cell culture supernatants contg. antigen selected from EspA, EspB, EspD, Tir and Intimin. The immune adjuvant is an oil-in-water emulsion comprising mineral oil and dimethyldioctadecylammonium bromide, or VSA3.

IC ICM A61K039-108
 ICS C07K014-245; C12N001-20; A61P031-04; A61K039-39; C07K001-02; C07K001-34

CC 15-2 (Immunochemistry)

Section cross-reference(s): 1, 3, 17, 63
 ST enterohemorrhagic Escherichia coli EspA EspB EspD Tir
 Intimin; vaccine enterohemorrhagic Escherichia coli adjuvant

IT Antigens
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (EspA; vaccine compns. comprising nucleic acid-based or recombinant proteins of enterohemorrhagic Escherichia coli EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)

IT Antigens
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (EspB; vaccine compns. comprising nucleic acid-based or recombinant proteins of enterohemorrhagic Escherichia coli EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)

- IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(EspD; vaccine compns. comprising nucleic acid-based or recombinant proteins of **enterohemorrhagic Escherichia coli** EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)
- IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Tir; vaccine compns. comprising nucleic acid-based or recombinant proteins of **enterohemorrhagic Escherichia coli** EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)
- IT Immunostimulants
(adjuvants, VSA3; vaccine compns. comprising nucleic acid-based or recombinant proteins of **enterohemorrhagic Escherichia coli** EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)
- IT Immunostimulants
(adjuvants; vaccine compns. comprising nucleic acid-based or recombinant proteins of **enterohemorrhagic Escherichia coli** EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)
- IT Health products
(biologicals; vaccine compns. comprising nucleic acid-based or recombinant proteins of **enterohemorrhagic Escherichia coli** EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)
- IT Meat
(contamination prevention; vaccine compns. comprising nucleic acid-based or recombinant proteins of **enterohemorrhagic Escherichia coli** EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)
- IT Water pollution
(control; vaccine compns. comprising nucleic acid-based or recombinant proteins of **enterohemorrhagic Escherichia coli** EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)
- IT Antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**enterohemorrhagic Escherichia coli**; vaccine compns. comprising nucleic acid-based or recombinant proteins of **enterohemorrhagic Escherichia coli** EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)
- IT Escherichia coli
(**enterohemorrhagic**, EHEC O157:H7 and EHEC O157:NM; vaccine compns. comprising nucleic acid-based or recombinant proteins of **enterohemorrhagic Escherichia coli** EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)
- IT Proteins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(intimins; vaccine compns. comprising nucleic acid-based or recombinant proteins of **enterohemorrhagic Escherichia coli** EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)
- IT Emulsions
(oil-in-water; vaccine compns. comprising nucleic acid-based or recombinant proteins of **enterohemorrhagic Escherichia coli** EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)
- IT Environmental pollution
(prevention; vaccine compns. comprising nucleic acid-based or recombinant proteins of **enterohemorrhagic Escherichia coli** EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)
- IT Proteins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(recombinant; vaccine compns. comprising nucleic acid-based or recombinant proteins of enterohemorrhagic Escherichia coli EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)

IT Antibacterial agents

Cattle

Dairy cattle

Human

Mammalia

Ruminant

Sheep

Vaccines

(vaccine compns. comprising nucleic acid-based or recombinant proteins of enterohemorrhagic Escherichia coli EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)

IT Fusion proteins (chimeric proteins)

Nucleic acids

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(vaccine compns. comprising nucleic acid-based or recombinant proteins of enterohemorrhagic Escherichia coli EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)

IT Hydrocarbon oils

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(vaccine compns. comprising nucleic acid-based or recombinant proteins of enterohemorrhagic Escherichia coli EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)

IT 148513-91-1, GenBank Z21555 158159-24-1, GenBank U5681 168665-22-3, GenBank U32312 178084-52-1, GenBank U59502 178084-53-2, GenBank U59503 178084-54-3, GenBank U59504 182910-74-3, GenBank X96953 183226-27-9, GenBank X99670 183226-28-0, GenBank Y09228 188795-33-7, GenBank U66102 207529-05-3, GenBank AF045568 207667-05-8, GenBank Y13068 209889-72-5, GenBank AF70067 209889-73-6, GenBank AF070068 209889-74-7, GenBank AF070069 211394-99-9, GenBank Y13859 212685-11-5, GenBank AJ225015 212685-13-7, GenBank AJ225018 212685-14-8, GenBank AJ225019 212685-15-9, GenBank AJ225020 212686-21-0, GenBank AJ225021 217577-91-8, GenBank Y17874 218347-97-8, GenBank AF059713 222342-79-2, GenBank AF054421 224254-45-9, GenBank AF064683 224328-72-7, GenBank U65681 225600-15-7, GenBank AF130315 225600-40-8, GenBank AF132728 225633-42-1, GenBank AF125993 225637-33-2, GenBank AB026719 225756-53-6, GenBank AF144008 225756-54-7, GenBank AF144009 244699-47-6, GenBank AF113597 252167-04-7, GenBank U38618 273190-25-3, GenBank AB036053 300654-38-0, GenBank AF301015 311759-93-0, GenBank AF319597 315175-73-6, GenBank AF329681 318227-92-8 318230-62-5 318230-63-6 318230-64-7 318230-65-8 318230-66-9 318230-67-0 318230-68-1 318230-69-2 318230-70-5 318232-09-6, GenBank AE005594 318232-10-9, GenBank AE005595 328225-07-6, GenBank AP002566 329299-17-4, GenBank AF200363 335560-51-5, GenBank AF254454 335560-52-6, GenBank AF254456 354705-42-3, GenBank AJ308551 372396-60-6, GenBank AJ275089 372396-61-7, GenBank AJ275090 372396-62-8, GenBank AJ275091 372396-63-9, GenBank AJ275092 372396-64-0, GenBank AJ275093 372396-65-1, GenBank AJ275098 372396-66-2, GenBank AJ275100 372396-67-3, GenBank AJ275105 382356-98-1, GenBank AJ275094 382356-99-2, GenBank AJ275095 382357-00-8, GenBank AJ275096 382357-01-9, GenBank AJ275097 382357-02-0, GenBank AJ275099 382357-03-1, GenBank AJ275101 382357-04-2, GenBank AJ275102 382357-05-3, GenBank AJ275103 382357-06-4, GenBank AJ275104 382357-07-5, GenBank AJ275106 382357-08-6, GenBank AJ275107 382357-09-7, GenBank AJ275108 382357-10-0, GenBank AJ275109 382357-11-1, GenBank AJ275110 382357-12-2, GenBank AJ275111 382357-13-3, GenBank AJ275112 382357-14-4, GenBank AJ275113 382548-49-4, GenBank AF254455 382548-50-7, GenBank AF254457 385301-88-2, GenBank AJ225016 385301-89-3, GenBank AJ225017 385339-76-4, GenBank AF081182 385339-77-5, GenBank AF081183 389713-68-2, GenBank U80796 389713-69-3, GenBank U80908 391763-53-4, GenBank Z54352 392029-82-2, GenBank

AF013122 398115-64-5, GenBank AF022236 403467-34-5, GenBank AF339751
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(vaccine compns. comprising nucleic acid-based or recombinant
 proteins of enterohemorrhagic Escherichia coli
 EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)

IT 3700-67-2, Dimethyldioctadecylammonium bromide
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (vaccine compns. comprising nucleic acid-based or recombinant
 proteins of enterohemorrhagic Escherichia coli
 EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:603715 HCAPLUS

DOCUMENT NUMBER: 133:280269

TITLE: Human response to Escherichia coli O157:H7
 infection: antibodies to secreted virulence factors

AUTHOR(S): Li, Yuling; Frey, Elizabeth; Mackenzie, Andrew M. R.;
 Finlay, B. Brett

CORPORATE SOURCE: Biotechnology Laboratory, University of British
 Columbia, Vancouver, BC, V6T 1Z3, Can.

SOURCE: Infection and Immunity (2000), 68(9), 5090-5095
 CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Vaccination has been proposed for the prevention of disease due to
 enterohemorrhagic Escherichia coli (EHEC), but the
 immune response following human infection, including the choice of
 potential antigens, has not been well characterized. To study this, sera
 were obtained from five pediatric patients with acute diarrhea caused by
E. coli O157:H7 0, 8, and 60 days after hospitalization. These
 sera were used to examine the immune response to four different EHEC
 virulence factors: Tir (translocated intimin receptor, which is inserted
 into the host cell membrane), intimin (bacterial outer membrane protein
 which binds to Tir), EspA (secreted protein which forms filamentous
 structures on EHEC surface), and EspB (inserted into the host membrane and
 cytoplasm). The response to O157:H7 lipopolysaccharide was also exmd.
 Sera were assayed against purified recombinant proteins using immunoblot
 anal. and by ELISA to det. the sera's titers to each of the antigens in
 all patients. We found that there was little reaction to EspA, EspB, and
 intimin in the acute-phase sera, although there was some reactivity to
 Tir. By day 8, titers of antibody to all four virulence factors were
 present in all patients, with a very strong response against Tir (up to a
 titer of 1:256,000), esp. in hemolytic-uremic syndrome patients, and
 lesser strong responses to the other three antigens. The titer to the
 antigens 60 days after hospitalization was decreased but was still highest
 for Tir. These results suggest that there is a strong immune response to
 Tir, and to a lesser extent to the other three virulence factors,
 following EHEC disease, indicating that these bacterial mols. are
 potential vaccine candidates for preventing EHEC disease. They
 also suggest that bacterial virulence factors that are inserted into host
 cells during infection by type III secretion systems (Tir or EspB) are
 still recognized by the host immune response.

CC 15-2 (Immunochemistry)

ST Escherichia virulence factor antibody diarrhea

IT Proteins, specific or class

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)

(EspA; human antibody response to Escherichia coli O157:H7
 secreted virulence factors in relation to potential vaccine
 candidates)

IT Proteins, specific or class

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)

(EspB; human antibody response to *Escherichia coli* 0157:H7 secreted virulence factors in relation to potential vaccine candidates)

- IT Receptors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (Tir (translocated intimin receptor); human antibody response to *Escherichia coli* 0157:H7 secreted virulence factors in relation to potential vaccine candidates)
- IT *Escherichia coli*
 (enterohemorrhagic; human antibody response to *Escherichia coli* 0157:H7 secreted virulence factors in relation to potential vaccine candidates)
- IT Diarrhea
 Vaccines
 (human antibody response to *Escherichia coli* 0157:H7 secreted virulence factors in relation to potential vaccine candidates)
- IT Antibodies
 RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (human antibody response to *Escherichia coli* 0157:H7 secreted virulence factors in relation to potential vaccine candidates)
- IT Proteins, specific or class
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (intimin; human antibody response to *Escherichia coli* 0157:H7 secreted virulence factors in relation to potential vaccine candidates)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1999:326051 HCAPLUS
 DOCUMENT NUMBER: 130:333761
 TITLE: Pathogenic *Escherichia coli* intimin receptor
 Tir and gene tir and methods for detecting gene tir or
 Tir protein and for drug screening
 INVENTOR(S): Finlay, B. Brett; Kenny, Brendan; Devinney,
 Rebekah; Stein, Marcus
 PATENT ASSIGNEE(S): University of British Columbia, Can.
 SOURCE: PCT Int. Appl., 91 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9924576	A1	19990520	WO 1998-CA1042	19981110
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2309559	AA	19990520	CA 1998-2309559	19981110
AU 9911373	A1	19990531	AU 1999-11373	19981110
EP 1029054	A1	20000823	EP 1998-954076	19981110
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
JP 2001522605	T2	20011120	JP 2000-520570	19981110

PRIORITY APPLN. INFO.:

US 1997-65130P P 19971112
 WO 1998-CA1042 W 19981110

- AB A polypeptide, called Tir (for translocated intimin receptor), which is secreted by attaching and effacing pathogens, such as the enteropathogenic (EPEC) and enterohemorrhagic (EHEC) *E. coli* is disclosed. These bacterial pathogens insert their own receptors into mammalian cell surfaces, to which the bacterial pathogen then adheres to trigger addnl. host signaling events and actin nucleation. Diagnosis of disease caused by pathogenic *E. coli* can be performed by the use of antibodies which bind to Tir to detect the protein or the use of nucleic acid probes for detection of nucleic acids encoding Tir polypeptide. Isolated nucleic acid sequences encoding Tir polypeptide, Tir peptides, a recombinant method for producing recombinant Tir, antibodies which bind to Tir, and a kit for the detection of Tir-producing *E. coli* are provided. A method of immunizing a host with Tir to induce a protective immune response to Tir or a second polypeptide of interest is also provided. A method for screening for compds. which interfere with the binding of bacterial pathogens to their receptors is further provided. Thus, protein Hp90, previously believed to be a host membrane protein, has been identified as an EHEC- or EPEC-secreted protein which acts as an intimin receptor. Proteins encoded by the espA and espB genes were necessary for delivery of Tir to the host membrane.
- IC ICM C12N015-31
 ICS C07K014-24; C07K016-12; G01N033-53; A61K038-16; C12Q001-68;
 C12N015-62
- CC 3-3 (Biochemical Genetics)
 Section cross-reference(s): 6, 10
- ST séquence enteropathogenic enterohemorrhagic Escherichia
 translocated intimin receptor gene tir; Hp90 EHEC EPEC gene tir intimin
 receptor
- IT Cattle
 (EHEC/EPEC vaccine for; pathogenic *Escherichia coli*
 intimin receptor Tir and gene tir and methods for detecting gene tir or
 Tir protein and for drug screening)
- IT *Escherichia coli*
 (EHEC/EPEC; pathogenic *Escherichia coli* intimin receptor Tir
 and gene tir and methods for detecting gene tir or Tir protein and for
 drug screening)
- IT Receptors
 RL: ANT (Analyte); BOC (Biological occurrence); BPN (Biosynthetic
 preparation); BPR (Biological process); BSU (Biological study,
 unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological
 study); OCCU (Occurrence); PREP (Preparation); PROC (Process)
 (Tir (translocated intimin receptor); pathogenic *Escherichia*
coli intimin receptor Tir and gene tir and methods for
 detecting gene tir or Tir protein and for drug screening)
- IT Antibodies
 RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
 (anti-Tir; pathogenic *Escherichia coli* intimin receptor Tir
 and gene tir and methods for detecting gene tir or Tir protein and for
 drug screening)
- IT Cytoskeleton
 (detection of, Tir for; pathogenic *Escherichia coli* intimin
 receptor Tir and gene tir and methods for detecting gene tir or Tir
 protein and for drug screening)
- IT Bacteria (Eubacteria)
 (espA-espB-, Tir fusion protein-producing, as immunogen; pathogenic
Escherichia coli intimin receptor Tir and gene tir and
 methods for detecting gene tir or Tir protein and for drug screening)
- IT Nucleic acid amplification (method)
 (for detection of tir gene; pathogenic *Escherichia coli*
 intimin receptor Tir and gene tir and methods for detecting gene tir or
 Tir protein and for drug screening)
- IT Proteins, specific or class
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (intimins, receptor; pathogenic *Escherichia coli* intimin
 receptor Tir and gene tir and methods for detecting gene tir or Tir

- IT protein and for drug screening)
IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(monoclonal, anti-Tir; pathogenic Escherichia coli intimin
receptor Tir and gene tir and methods for detecting gene tir or Tir
protein and for drug screening)
IT Protein sequences
(of gene tir intimin receptor of pathogenic Escherichia coli
EHEC and EPEC)
IT DNA sequences
(of intimin receptor gene tir of pathogenic Escherichia coli
EHEC and EPEC)
IT Molecular cloning
(of tir gene; pathogenic Escherichia coli intimin receptor
Tir and gene tir and methods for detecting gene tir or Tir protein and
for drug screening)
IT Drug screening
(pathogenic Escherichia coli intimin receptor Tir and gene
tir and methods for detecting gene tir or Tir protein and for drug
screening)
IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(pathogenic Escherichia coli intimin receptor Tir and gene
tir and methods for detecting gene tir or Tir protein and for drug
screening)
IT 200662-09-5P 224307-15-7P
RL: ANT (Analyte); BOC (Biological occurrence); BPN (Biosynthetic
preparation); BPR (Biological process); BSU (Biological study,
unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological
study); OCCU (Occurrence); PREP (Preparation); PROC (Process)
(amino acid sequence; pathogenic Escherichia coli intimin
receptor Tir and gene tir and methods for detecting gene tir or Tir
protein and for drug screening)
IT 200697-61-6, GenBank AF013122 224307-16-8
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological
study); USES (Uses)
(nucleotide sequence; pathogenic Escherichia coli intimin
receptor Tir and gene tir and methods for detecting gene tir or Tir
protein and for drug screening)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file medline
FILE 'MEDLINE' ENTERED AT 14:45:44 ON 10 OCT 2003

FILE LAST UPDATED: 9 OCT 2003 (20031009/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See <http://www.nlm.nih.gov/mesh/changes2003.html> for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que 111

L1	1944 SEA FILE=MEDLINE ABB=ON	PLU=ON	ESCHERICHIA COLI 0157/CT
L5	18878 SEA FILE=MEDLINE ABB=ON	PLU=ON	ADJUVANTS, IMMUNOLOGIC/CT
L11	1 SEA FILE=MEDLINE ABB=ON	PLU=ON	L1 AND L5

CT = controlled terminology
(indexing)

=> d que 130

L1	1944 SEA FILE=MEDLINE ABB=ON	PLU=ON	ESCHERICHIA COLI 0157/CT
L25	600759 SEA FILE=MEDLINE ABB=ON	PLU=ON	IMMUNITY+NT/CT
L26	71 SEA FILE=MEDLINE ABB=ON	PLU=ON	L1 AND L25
L30	1 SEA FILE=MEDLINE ABB=ON	PLU=ON	L26 AND SUPERNA?

NT = narrower term

=> d que 134

L1	1944 SEA FILE=MEDLINE ABB=ON	PLU=ON	ESCHERICHIA COLI 0157/CT
L25	600759 SEA FILE=MEDLINE ABB=ON	PLU=ON	IMMUNITY+NT/CT
L26	71 SEA FILE=MEDLINE ABB=ON	PLU=ON	L1 AND L25
L33	26 SEA FILE=MEDLINE ABB=ON	PLU=ON	L26 AND ANTIGEN?
L34	1 SEA FILE=MEDLINE ABB=ON	PLU=ON	L33 AND ESPB/TI

1c.7e

=> s 111 or 130 or 134

L130 3 L11 OR L30 OR L34

3 cites for medline

=> file embase

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=> d que 147

L1	1944 SEA FILE=MEDLINE ABB=ON	PLU=ON	ESCHERICHIA COLI 0157/CT
L25	600759 SEA FILE=MEDLINE ABB=ON	PLU=ON	IMMUNITY+NT/CT
L26	71 SEA FILE=MEDLINE ABB=ON	PLU=ON	L1 AND L25
L30	1 SEA FILE=MEDLINE ABB=ON	PLU=ON	L26 AND SUPERNA?
L41	443 SEA FILE=EMBASE ABB=ON	PLU=ON	L30 OR EHEC
L42	1967 SEA FILE=EMBASE ABB=ON	PLU=ON	0157
L44	2149 SEA FILE=EMBASE ABB=ON	PLU=ON	L41 OR L42
L45	4879 SEA FILE=EMBASE ABB=ON	PLU=ON	IMMUN?(4A)ADJUVANT
L46	4 SEA FILE=EMBASE ABB=ON	PLU=ON	L44 AND L45
L47	3 SEA FILE=EMBASE ABB=ON	PLU=ON	L46 NOT DEXTRAN/TI

3 cites

=> d que 150

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L1      1944 SEA FILE=MEDLINE ABB=ON PLU=ON ESCHERICHIA COLI 0157/CT
L25     600759 SEA FILE=MEDLINE ABB=ON PLU=ON IMMUNITY+NT/CT
L26     71 SEA FILE=MEDLINE ABB=ON PLU=ON L1 AND L25
L30     1 SEA FILE=MEDLINE ABB=ON PLU=ON L26 AND SUPERNA?
L41     443 SEA FILE=EMBASE ABB=ON PLU=ON L30 OR EHEC
L42     1967 SEA FILE=EMBASE ABB=ON PLU=ON 0157
L44     2149 SEA FILE=EMBASE ABB=ON PLU=ON L41 OR L42
L49     10 SEA FILE=EMBASE ABB=ON PLU=ON L44 AND OIL
L50     1 SEA FILE=EMBASE ABB=ON PLU=ON L49 AND DELIVERY/TI    1 cite
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=> d que 159

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L1      1944 SEA FILE=MEDLINE ABB=ON PLU=ON ESCHERICHIA COLI 0157/CT
L25     600759 SEA FILE=MEDLINE ABB=ON PLU=ON IMMUNITY+NT/CT
L26     71 SEA FILE=MEDLINE ABB=ON PLU=ON L1 AND L25
L30     1 SEA FILE=MEDLINE ABB=ON PLU=ON L26 AND SUPERNA?
L41     443 SEA FILE=EMBASE ABB=ON PLU=ON L30 OR EHEC
L42     1967 SEA FILE=EMBASE ABB=ON PLU=ON 0157
L44     2149 SEA FILE=EMBASE ABB=ON PLU=ON L41 OR L42
L57     40 SEA FILE=EMBASE ABB=ON PLU=ON L44 AND SUPERNA?
L58     5 SEA FILE=EMBASE ABB=ON PLU=ON L57 AND ANTIGEN?
L59     1 SEA FILE=EMBASE ABB=ON PLU=ON L58 AND PHAGES/TI    1 cite
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=> s 147 or 150 or 159

L131 4 L47 OR L50 OR L59 4 cites for embase

=> file uspatfull

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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 9 Oct 2003 (20031009/PD)
FILE LAST UPDATED: 9 Oct 2003 (20031009/ED)
HIGHEST GRANTED PATENT NUMBER: US6631523
HIGHEST APPLICATION PUBLICATION NUMBER: US2003192101
CA INDEXING IS CURRENT THROUGH 9 Oct 2003 (20031009/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 9 Oct 2003 (20031009/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2003

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>>> USPAT2 is now available. USPATFULL contains full text of the      <<<
>>> original, i.e., the earliest published granted patents or      <<<
>>> applications. USPAT2 contains full text of the latest US      <<<
>>> publications, starting in 2001, for the inventions covered in      <<<
>>> USPATFULL. A USPATFULL record contains not only the original      <<<
>>> published document but also a list of any subsequent      <<<
>>> publications. The publication number, patent kind code, and      <<<
>>> publication date for all the US publications for an invention      <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL      <<<
>>> records and may be searched in standard search fields, e.g., /PN,      <<<
>>> /PK, etc.                                              <<<

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>>> enter this cluster.                                              <<<
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>>> classifications, or claims, that may potentially change from      <<<
>>> the earliest to the latest publication.                                              <<<
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=> d que l115

L108	62349 SEA FILE=USPATFULL ABB=ON	PLU=ON	(E OR ESCHERICHIA)(W)COLI
L110	449 SEA FILE=USPATFULL ABB=ON	PLU=ON	L108(5A) ENTEROHEM?
L114	626 SEA FILE=USPATFULL ABB=ON	PLU=ON	(EHEC OR O157-H7 OR O157-NM)
L115	1 SEA FILE=USPATFULL ABB=ON	PLU=ON	(L114 OR L110)(5A)ADJUVANT

1 patient

=> d que l119

L107	335 SEA FILE=USPATFULL ABB=ON	PLU=ON	DIMETHYLDIOCTADECYLAMMONIUM
L108	62349 SEA FILE=USPATFULL ABB=ON	PLU=ON	(E OR ESCHERICHIA)(W)COLI
L110	449 SEA FILE=USPATFULL ABB=ON	PLU=ON	L108(5A) ENTEROHEM?
L114	626 SEA FILE=USPATFULL ABB=ON	PLU=ON	(EHEC OR O157-H7 OR O157-NM)
L116	195 SEA FILE=USPATFULL ABB=ON	PLU=ON	(L114 OR L110)(P)ADJUVANT
L117	188 SEA FILE=USPATFULL ABB=ON	PLU=ON	L116 AND (L107 OR EMULSION OR VSA3)
L118	36 SEA FILE=USPATFULL ABB=ON	PLU=ON	(EHEC OR O157-H7 OR O157-NM)/AB
L119	1 SEA FILE=USPATFULL ABB=ON	PLU=ON	L118 AND L117

1 patient

=> d que l129

L108	62349 SEA FILE=USPATFULL ABB=ON	PLU=ON	(E OR ESCHERICHIA)(W)COLI
L110	449 SEA FILE=USPATFULL ABB=ON	PLU=ON	L108(5A) ENTEROHEM?
L114	626 SEA FILE=USPATFULL ABB=ON	PLU=ON	(EHEC OR O157-H7 OR O157-NM)
L121	145 SEA FILE=USPATFULL ABB=ON	PLU=ON	(L114 OR L110) AND IMMUNOSTI M?
L122	144 SEA FILE=USPATFULL ABB=ON	PLU=ON	L121 AND VACCIN?
L123	142 SEA FILE=USPATFULL ABB=ON	PLU=ON	L122 AND (CELL CULTUR? OR SUPERN?)
L124	142 SEA FILE=USPATFULL ABB=ON	PLU=ON	L123 AND ANTIGEN?
L125	7201 SEA FILE=USPATFULL ABB=ON	PLU=ON	((E/CLM OR ESCHERICHIA/CLM)(W)COLI/CLM)
L126	1456 SEA FILE=USPATFULL ABB=ON	PLU=ON	((E/AB OR ESCHERICHIA/AB)(W) COLI/AB)
L127	7678 SEA FILE=USPATFULL ABB=ON	PLU=ON	L125 OR L126
L128	156 SEA FILE=USPATFULL ABB=ON	PLU=ON	L127 AND (EHEC OR O157-H7 OR O157-NM OR ?HEMMOR?)
L129	2 SEA FILE=USPATFULL ABB=ON	PLU=ON	L128 AND L124

2 patients

=> s l115 or l119 or l129

L132	3 L115 OR L119 OR L129	3 patients total from USPATFUL
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=> file hcaplus

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FILE LAST UPDATED: 9 Oct 2003 (20031009/ED)

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=> d que 179

L69	216721 SEA FILE=HCAPLUS ABB=ON	PLU=ON	ESCHERICHIA COLI
L70	1968 SEA FILE=HCAPLUS ABB=ON	PLU=ON	L69(L)(EHEC OR ENTEROHEM? OR 0157-H7)
L78	24998 SEA FILE=HCAPLUS ABB=ON	PLU=ON	EMULSIONS/CT
L79	2 SEA FILE=HCAPLUS ABB=ON	PLU=ON	L78 AND L70

2 cites

=> d que 187

L69	216721 SEA FILE=HCAPLUS ABB=ON	PLU=ON	ESCHERICHIA COLI
L70	1968 SEA FILE=HCAPLUS ABB=ON	PLU=ON	L69(L)(EHEC OR ENTEROHEM? OR 0157-H7)
L85	872 SEA FILE=HCAPLUS ABB=ON	PLU=ON	3700-67-2/RN OR DIMETHYLDIOCTA DECYLAMMONIUM BROMIDE
L87	1 SEA FILE=HCAPLUS ABB=ON	PLU=ON	L85 AND L70

2 cites

=> d que 189

L69	216721 SEA FILE=HCAPLUS ABB=ON	PLU=ON	ESCHERICHIA COLI
L70	1968 SEA FILE=HCAPLUS ABB=ON	PLU=ON	L69(L)(EHEC OR ENTEROHEM? OR 0157-H7)
L88	5 SEA FILE=HCAPLUS ABB=ON	PLU=ON	VSA3 OR VSA-3
L89	1 SEA FILE=HCAPLUS ABB=ON	PLU=ON	L88 AND L70

1 cite

=> d que 196

L69	216721 SEA FILE=HCAPLUS ABB=ON	PLU=ON	ESCHERICHIA COLI
L70	1968 SEA FILE=HCAPLUS ABB=ON	PLU=ON	L69(L)(EHEC OR ENTEROHEM? OR 0157-H7)
L94	12 SEA FILE=HCAPLUS ABB=ON	PLU=ON	L70 AND ADJUVANT
L95	6 SEA FILE=HCAPLUS ABB=ON	PLU=ON	L94 AND VACCINE/OBI
L96	1 SEA FILE=HCAPLUS ABB=ON	PLU=ON	L95 AND GLYCOCOCONJUGAT?/TI

1 cite

OBI = all search fields except the abstract

=> s 179 or 187 or 189 or 196

L133 3 L79 OR L87 OR L89 OR L96 3 cites for HCA PLUS

=> file wpids

FILE 'WPIDS' ENTERED AT 14:45:57 ON 10 OCT 2003
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FILE LAST UPDATED: 9 OCT 2003 <20031009/UP>
MOST RECENT DERWENT UPDATE: 200365 <200365/DW>
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=> d que l103

L97	13924 SEA FILE=WPIDS ABB=ON	PLU=ON	(E OR ESCHERICHIA) (W) COLI
L98	96 SEA FILE=WPIDS ABB=ON	PLU=ON	L97 AND (EHEC OR 0157-H7 OR 0157-NM)
L99	51 SEA FILE=WPIDS ABB=ON	PLU=ON	L97 AND ENTEROHEM?
L100	117 SEA FILE=WPIDS ABB=ON	PLU=ON	(L98 OR L99)
L102	39 SEA FILE=WPIDS ABB=ON	PLU=ON	DIMETHYLDIOCTADECYLAMMONIUM
L103	1 SEA FILE=WPIDS ABB=ON	PLU=ON	L102 AND L100 <i>1 cite</i>

=> d que l105

L97	13924 SEA FILE=WPIDS ABB=ON	PLU=ON	(E OR ESCHERICHIA) (W) COLI
L98	96 SEA FILE=WPIDS ABB=ON	PLU=ON	L97 AND (EHEC OR 0157-H7 OR 0157-NM)
L99	51 SEA FILE=WPIDS ABB=ON	PLU=ON	L97 AND ENTEROHEM?
L100	117 SEA FILE=WPIDS ABB=ON	PLU=ON	(L98 OR L99)
L105	1 SEA FILE=WPIDS ABB=ON	PLU=ON	L100 AND VSA3 <i>1 cite</i>

=> s l103 or l105

L134 1 L103 OR L105 *1 cite for WPDS (applicant)*
=> dup rem l130 l131 l132 l133 l134 *removing duplicate cites*
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PROCESSING COMPLETED FOR L131
PROCESSING COMPLETED FOR L132
PROCESSING COMPLETED FOR L133
PROCESSING COMPLETED FOR L134

L135 13 DUP REM L130 L131 L132 L133 L134 (1 DUPLICATE REMOVED)
ANSWERS '1-3' FROM FILE MEDLINE
ANSWERS '4-7' FROM FILE EMBASE
ANSWERS '8-10' FROM FILE USPATFULL
ANSWERS '11-13' FROM FILE HCAPLUS

13 cites total

=> d ibib abs ind 1-7
L135 ANSWER 1 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2001408711 MEDLINE

DOCUMENT NUMBER: 21127279 PubMed ID: 11228378
 TITLE: Nasal immunization with *E. coli* verotoxin 1 (VT1)-B subunit and a nontoxic mutant of cholera toxin elicits serum neutralizing antibodies.
 AUTHOR: Byun Y; Ohmura M; Fujihashi K; Yamamoto S; McGhee J R;
 Udaka S; Kiyono H; Takeda Y; Kohsaka T; Yuki Y
 CORPORATE SOURCE: JCR Biopharmaceuticals Incorporated, , San Diego, CA 92121-1194, USA.
 CONTRACT NUMBER: AI 18958 (NIAID)
 AI 35932 (NIAID)
 AI 43197 (NIAID)
 AI 65298 (NIAID)
 AI 65299 (NIAID)
 DE 09837 (NIDCR)
 DE 12242 (NIDCR)
 DK 44240 (NIDDK)
 SOURCE: VACCINE, (2001 Feb 28) 19 (15-16) 2061-70.
 Journal code: 8406899. ISSN: 0264-410X.
 PUB. COUNTRY: England: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200107
 ENTRY DATE: Entered STN: 20010723
 Last Updated on STN: 20010723
 Entered Medline: 20010719

AB Escherichia coli O157:H7 produces two forms of verotoxin (VT), VT1 and VT2, which cause hemorrhagic colitis with development, in some cases, of hemolytic uremic syndrome. These toxins consist of an enzymatically active A subunit and pentamers of B subunit responsible for their binding to host cells. We used the secretion-expression system of *Bacillus brevis* to produce recombinant VT1B and VT2B. The secreted B subunits were purified and sequenced to verify their structure. Receptor-binding showed that rVT1B but not rVT2B bound to Gb3-receptor. When mice were nasally immunized with rVT1B or rVT2B together with a nontoxic mutant of cholera toxin (mCT) or native cholera toxin (nCT) as adjuvants, serum IgG and mucosal IgA antibody responses to VT1B were induced. The VT1B-specific antibodies prevented VT1B binding to its Gb3 receptor. In contrast, poor serum and no mucosal VT2B-specific antibodies but brisk CTB-specific antibody responses were induced by nasal immunization with rVT2B in the presence of mCT or nCT. These results show that nasal immunization with rVTB and mCT as a nontoxic mucosal adjuvant is an effective regimen for the induction of VT1B but not VT2B antibody responses which inhibit VT1B binding to Gb3 receptor.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
 Adjuvants, Immunologic: AD, administration & dosage
 Administration, Intranasal
 Amino Acid Sequence
 *Antibodies, Bacterial: BL, blood
 Bacillus: GE, genetics
 Bacterial Vaccines: AD, administration & dosage
 Bacterial Vaccines: GE, genetics
 Bacterial Vaccines: IM, immunology
 Base Sequence
 *Cholera Toxin: AD, administration & dosage
 Cholera Toxin: GE, genetics
 Cholera Toxin: TO, toxicity
 DNA Primers: GE, genetics
 Escherichia coli O157: IM, immunology
 Genetic Vectors
 Mice
 Mice, Inbred BALB C
 Molecular Sequence Data
 Neutralization Tests
 Plasmids: GE, genetics
 Protein Subunits
 *Shiga-Like Toxin I: AD, administration & dosage

Shiga-Like Toxin I: CH, chemistry
 Shiga-Like Toxin I: GE, genetics
 Shiga-Like Toxin II: AD, administration & dosage
 Shiga-Like Toxin II: GE, genetics
 Vaccines, Synthetic: AD, administration & dosage
 Vaccines, Synthetic: GE, genetics
 Vaccines, Synthetic: IM, immunology
 RN 9012-63-9 (Cholera Toxin)
 CN 0 (Adjuvants, Immunologic); 0 (Antibodies, Bacterial); 0 (Bacterial Vaccines); 0 (DNA Primers); 0 (Genetic Vectors); 0 (Plasmids); 0 (Protein Subunits); 0 (Shiga-Like Toxin I); 0 (Shiga-Like Toxin II); 0 (Vaccines, Synthetic)

L135 ANSWER 2 OF 13 MEDLINE on STN
 ACCESSION NUMBER: 2000278163 MEDLINE
 DOCUMENT NUMBER: 20278163 PubMed ID: 10816529
 TITLE: Role of EspB in experimental human enteropathogenic Escherichia coli infection.
 AUTHOR: Tacket C O; Sztein M B; Losonsky G; Abe A; Finlay B B; McNamara B P; Fantry G T; James S P; Nataro J P; Levine M M; Donnenberg M S
 CORPORATE SOURCE: Center for Vaccine Development, Department of Medicine, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA.. ctacket@medicine.umaryland.edu
 CONTRACT NUMBER: AI32074 (NIAID)
 N01-AI-65299 (NIAID)
 SOURCE: INFECTION AND IMMUNITY, (2000 Jun) 68 (6) 3689-95.
 Journal code: 0246127. ISSN: 0019-9567.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: (CLINICAL TRIAL)
 Journal; Article; (JOURNAL ARTICLE)
 (RANDOMIZED CONTROLLED TRIAL)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200006
 ENTRY DATE: Entered STN: 20000706
 Last Updated on STN: 20000706
 Entered Medline: 20000623

AB Enteropathogenic Escherichia coli (EPEC), a leading cause of diarrhea among infants in developing countries, induces dramatic alterations in host cell architecture that depend on a type III secretion system. EspB, one of the proteins secreted and translocated to the host cytoplasm via this system, is required for numerous alterations in host cell structure and function. To determine the role of EspB in virulence, we conducted a randomized, double-blind trial comparing the ability of wild-type EPEC and an isogenic DeltaespB mutant strain to cause diarrhea in adult volunteers. Diarrhea developed in 9 of 10 volunteers who ingested the wild-type strain but in only 1 of 10 volunteers who ingested the DeltaespB mutant strain. Marked destruction of the microvillous brush border adjacent to adherent organisms was observed in a jejunal biopsy from a volunteer who ingested the wild-type strain but not from two volunteers who ingested the DeltaespB mutant strain. Humoral and cell-mediated immune responses to EPEC antigens were stronger among recipients of the wild-type strain. In addition, four of the volunteers who ingested the wild-type strain had lymphoproliferative responses to EspB. These results demonstrate that EspB is a critical virulence determinant of EPEC infections and suggest that EspB contributes to an immune response.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
 Adolescent
 Adult
 Antibodies, Bacterial: BL, blood
 *Bacterial Outer Membrane Proteins: GE, genetics
 Biopsy
 Diarrhea: IM, immunology
 *Diarrhea: MI, microbiology
 Double-Blind Method
 *Escherichia coli: PY, pathogenicity

Escherichia coli Infections: IM, immunology
 *Escherichia coli Infections: MI, microbiology
 Escherichia coli O157: PY, pathogenicity
 Immunity, Cellular
 Interferon Type II: BI, biosynthesis
 Jejunum: MI, microbiology
 Jejunum: PA, pathology
 Microvilli: PA, pathology
 Vaccination
 RN 82115-62-6 (Interferon Type II)
 CN 0 (Antibodies, Bacterial); 0 (Bacterial Outer Membrane Proteins); 0 (EaeB protein)

L135 ANSWER 3 OF 13 MEDLINE on STN
 ACCESSION NUMBER: 1999120390 MEDLINE
 DOCUMENT NUMBER: 99120390 PubMed ID: 9923515
 TITLE: Strain-specific differences in the amount of Shiga toxin released from enterohemorrhagic Escherichia coli O157 following exposure to subinhibitory concentrations of antimicrobial agents.
 AUTHOR: Grif K; Dierich M P; Karch H; Allerberger F
 CORPORATE SOURCE: Institute of Hygiene, University of Innsbruck, Austria.
 SOURCE: EUROPEAN JOURNAL OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES, (1998 Nov) 17 (11) 761-6.
 Journal code: 8804297. ISSN: 0934-9723.
 PUB. COUNTRY: GERMANY: Germany, Federal Republic of
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199904
 ENTRY DATE: Entered STN: 19990504
 Last Updated on STN: 20021026
 Entered Medline: 19990420

AB There is no consensus regarding the benefit versus harm of antibiotic therapy for treatment of disease due to enterohemorrhagic Escherichia coli O157. The effects in vitro of subinhibitory concentrations of 13 antimicrobial agents on the release of Shiga toxin (Stx) by three different Escherichia coli O157 strains expressing Stx 1 or Stx 2 either alone or in combination were investigated. The Stx-induced cell death of Vero cells was determined using a colorimetric assay based on the measurement of lactate dehydrogenase (LDH) released into the supernatant from the cytosol of damaged cells. Growth of all O157 strains in broth cultures containing subinhibitory concentrations of cotrimoxazole, trimethoprim, azithromycin, or gentamicin was accompanied by a marked increase in the release of Stx. Exposure to cefixime, ceftriaxone, or erythromycin caused a marked increase in the release of Stx by the O157 strain producing Stx 2 alone, but decreased toxin production was observed with the Stx 1 producer and the strain producing Stx 1 and Stx 2. Exposure to ampicillin caused increased Stx release in the Stx 2-producing strain but had no effect on Stx production in the other two test isolates. Exposure to penicillin G, streptomycin, ciprofloxacin, fosfomycin, or sulfamethoxazole caused an increase in toxin production in two of the three test strains in each case, while decreases were observed for the other isolates. The response of Escherichia coli O157 isolates to subinhibitory concentrations of antibiotics seems to be highly dependent on the nature of the strain involved.

CT Check Tags: Animal; Comparative Study; Human; Support, Non-U.S. Gov't
 *Antibiotics: PD, pharmacology
 *Bacterial Toxins: BI, biosynthesis
 Cercopithecus aethiops
 Escherichia coli Infections: CO, complications
 Escherichia coli Infections: MI, microbiology
 *Escherichia coli O157: DE, drug effects
 *Escherichia coli O157: ME, metabolism
 Hemolytic-Uremic Syndrome: MI, microbiology
 Lactate Dehydrogenase: ME, metabolism
 Shiga Toxins

Species Specificity

Vero Cells

CN 0 (Antibiotics); 0 (Bacterial Toxins); 0 (Shiga Toxins); EC 1.1.1.27
(Lactate Dehydrogenase)L135 ANSWER 4 OF 13 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2002222994 EMBASE

TITLE: Mucosal immunoadjuvant activity of the low toxic recombinant Escherichia coli heat-labile enterotoxin produced by Bacillus brevis for the bacterial subunit or component vaccine in pigs and cattle.

AUTHOR: Yokomizo Y.; Watanabe F.; Imada Y.; Inumaru S.; Yanaka T.; Tsuji T.

CORPORATE SOURCE: Y. Yokomizo, National Institute of Animal Health, Kannondai 3-1-5, Ibarakiken, Japan. yokomi@affrc.go.jp

SOURCE: Veterinary Immunology and Immunopathology, (2002) 87/3-4 (291-300).

Refs: 20

ISSN: 0165-2427 CODEN: VIIMDS

PUBLISHER IDENT.: S 0165-2427(02)00055-7

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A gene encoding the mature Escherichia coli heat-labile enterotoxin (LT) lacking the nick site in the A subunit by deleting tripeptides was introduced in a vector pNH301 and expressed extracellularly as mutant molecule of holotoxin at high levels in Bacillus brevis HPD31-S5 of the host bacterium. The mucosal adjuvant activities of the produced mutant LT (mLT) preparation were studied in pigs and cattle. Intranasal immunization of pigs with the recombinant subunit vaccine of *Erysipelothrix rhusiopathiae* or the component vaccine of *Bordetella bronchiseptica* mixed with the mLT resulted in a substantial enhancement of both mucosal and serum-specific antibody levels. The immunized pigs were also protected when challenge-exposed intradermally with a highly virulent *E. rhusiopathiae* strain or challenge-exposed intranasally with a highly virulent strain of *B. bronchiseptica*. The mLT intranasally administered with recombinant intimin (an outer membrane adhesin) of *E. coli* O157:H7 also induced an elevation of IgA-specific antibody in the nasal secretion and saliva of calves as well as an elevation of IgG1-specific antibody level against the intimin in the sera and colostrum of cows. The three kinds tested protein antigens were poorly immunogenic when antigen administered intranasally alone. The mLT intranasally administered at a higher effective dose did not induce local adverse reactions or diarrhea in pigs and cattle. The present study demonstrates that the recombinant mLT produced using the *B. brevis* expression system might represent promising immunoadjuvants for the potential application of intranasal vaccines directed against infectious diseases in pigs and cattle. .COPYRGT. 2002 Elsevier Science B.V. All rights reserved.

CT Medical Descriptors:

*immunization

Escherichia coli

Bacillus brevis

swine

cattle

saliva

colostrum

cow

infection: DT, drug therapy

infection: ET, etiology

infection: PC, prevention

nonhuman

animal experiment

animal model

controlled study

conference paper

Drug Descriptors:

- *immunological adjuvant: DT, drug therapy
- *immunological adjuvant: PD, pharmacology
- *immunological adjuvant: NA, intranasal drug administration
- *Escherichia coli vaccine: DT, drug therapy
- *Escherichia coli vaccine: PD, pharmacology
- *Escherichia coli vaccine: NA, intranasal drug administration
- *erysipelothrix vaccine: DT, drug therapy
- *erysipelothrix vaccine: PD, pharmacology
- *erysipelothrix vaccine: NA, intranasal drug administration
- *bordetella bronchiseptica vaccine: DT, drug therapy
- *bordetella bronchiseptica vaccine: PD, pharmacology
- *bordetella bronchiseptica vaccine: NA, intranasal drug administration
- *bacterial vaccine: DT, drug therapy
- *bacterial vaccine: PD, pharmacology
- *bacterial vaccine: NA, intranasal drug administration
- unclassified drug

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ACCESSION NUMBER: 2001303614 EMBASE

TITLE: Intimin-specific immune responses prevent bacterial colonization by the attaching-effacing pathogen *Citrobacter rodentium*.

AUTHOR: Ghaem-Maghami M.; Simmons C.P.; Daniell S.; Pizza M.; Lewis D.; Frankel G.; Dougan G.

CORPORATE SOURCE: C.P. Simmons, Department of Biochemistry, Imperial Coll. Sci., Technol./Med., South Kensington, London SW7 2AZ, United Kingdom. c.simmons@ic.ac.uk

SOURCE: Infection and Immunity, (2001) 69/9 (5597-5605).

Refs: 45

ISSN: 0019-9567 CODEN: INFIBR

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

026 Immunology, Serology and Transplantation

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The formation of attaching and effacing (A/E) lesions on gut enterocytes is central to the pathogenesis of enterohemorrhagic (EHEC) *Escherichia coli*, enteropathogenic *E. coli* (EPEC), and the rodent pathogen *Citrobacter rodentium*. Genes encoding A/E lesion formation map to a chromosomal pathogenicity island termed the locus of enterocyte effacement (LEE). Here we show that the LEE-encoded proteins EspA, EspB, Tir, and intimin are the targets of long-lived humoral immune responses in *C. rodentium*-infected mice. Mice infected with *C. rodentium* developed robust acquired immunity and were resistant to reinfection with wild-type *C. rodentium* or a *C. rodentium* derivative, DBS255(pCVD438), which expressed intimin derived from EPEC strain E2348/69. The receptor-binding domain of intimin polypeptides is located within the carboxy-terminal 280 amino acids (Int280). Mucosal and systemic vaccination regimens using enterotoxin-based adjuvants were employed to elicit immune responses to recombinant Int280.alpha. from EPEC strain E2348/69. Mice vaccinated subcutaneously with Int280.alpha., in the absence of adjuvant, were significantly more resistant to oral challenge with DBS255(pCVD438) but not with wild-type *C. rodentium*. This type-specific immunity could not be overcome by employing an exposed, highly conserved domain of intimin (Int(388-667)) as a vaccine. These results show that anti-intimin immune responses can modulate the outcome of a *C. rodentium* infection and support the use of intimin as a component of a type-specific EPEC or EHEC vaccine.

CT Medical Descriptors:

- **Citrobacter*
- **citrobacter rodentium*
- *bacterial colonization

humoral immunity
 gene function
 reinfection
 infection resistance
 protein domain
 protein analysis
Escherichia coli
 vaccination
 Gram negative infection: DT, drug therapy
 Gram negative infection: ET, etiology
 Gram negative infection: PC, prevention
 treatment outcome
 nonhuman
 female
 mouse
 animal experiment
 animal model
 controlled study
 article
 priority journal
Drug Descriptors:
 *intimin: DV, drug development
 *intimin: DO, drug dose
 *intimin: DT, drug therapy
 *intimin: SC, subcutaneous drug administration
 *intimin [388-667]: DV, drug development
 *intimin [388-667]: DO, drug dose
 *intimin [388-667]: DT, drug therapy
 *intimin [388-667]: SC, subcutaneous drug administration
 protein espA
 protein espB
 protein Tir
 gene product
 enterotoxin
 adjuvant
 unclassified drug

L135 ANSWER 6 OF 13 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
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ACCESSION NUMBER: 2002050356 EMBASE
 TITLE: Advances in vaccine delivery.
 AUTHOR: Mishra P.R.; Jain N.K.
 CORPORATE SOURCE: N.K. Jain, Dept. of Pharmaceutical Sciences, Dr. H.S.Gour
University, Sagar (M.P.) 470 003, India
 SOURCE: Indian Drugs, (2001) 38/10 (493-501).
 Refs: 75
 ISSN: 0019-462X CODEN: INDRBA

COUNTRY: India
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT:
 037 Drug Literature Index
 026 Immunology, Serology and Transplantation
 030 Pharmacology
 039 Pharmacy
 038 Adverse Reactions Titles
 004 Microbiology
 022 Human Genetics

LANGUAGE: English
 SUMMARY LANGUAGE: English
 AB Vaccine consists of proteins and peptides either purified from natural sources or produced by recombinant DNA methodology or even by chemical peptide synthesis. Recent advances in 'new vaccine', is based on the development of vaccine adjuvants which enhances the overall immunogenicity of purified antigens. The immunological adjuvant plays a key role in the delivery of vaccines and is composed of whole, inactivated microorganisms, which are unable to replicate in the host. The immunological adjuvants help in enhancing the immunogenicity of these types of vaccines

through better antigen presentation. The present article is a brief review of various adjuvants used for vaccine delivery.

CT Medical Descriptors:

human
nonhuman
peptide synthesis
immunogenicity
genetic engineering and gene technology
microorganism
microbial growth
antigen presentation
drug delivery system
antigen presenting cell
immune system
drug classification
delayed hypersensitivity
cellular immunity
drug efficacy
immune response
physical chemistry
antibody response
medical technology
antibody titer
immunization
Gram negative infection: DT, drug therapy

Escherichia coli O157
Shigella flexneri
hepatitis A: DT, drug therapy
influenza: DT, drug therapy
hepatitis B: DT, drug therapy
diphtheria: DT, drug therapy
tetanus: DT, drug therapy
chill: SI, side effect
hypertension: SI, side effect
toxicity testing
drug formulation
review

Drug Descriptors:

*vaccine: PR, pharmaceutics
*vaccine: DV, drug development
*vaccine: DT, drug therapy
*vaccine: IM, intramuscular drug administration
*vaccine: PO, oral drug administration
*vaccine: PD, pharmacology
*vaccine: AE, adverse drug reaction
*vaccine: IP, intraperitoneal drug administration
*vaccine: AN, drug analysis
*vaccine: CB, drug combination
*vaccine: IT, drug interaction
 *immunological adjuvant: PD, pharmacology
 *immunological adjuvant: CM, drug comparison
 *immunological adjuvant: PR, pharmaceutics
 *immunological adjuvant: DV, drug development
 *immunological adjuvant: AE, adverse drug reaction
 *immunological adjuvant: DT, drug therapy
 *immunological adjuvant: IP, intraperitoneal drug administration
 *immunological adjuvant: AN, drug analysis
 *immunological adjuvant: CB, drug combination
 *immunological adjuvant: IT, drug interaction

recombinant DNA
protein
peptide
antigen: PR, pharmaceutics
antigen: DV, drug development
antigen: DT, drug therapy
antigen: IM, intramuscular drug administration
antigen: PO, oral drug administration

antigen: PD, pharmacology
antigen: TO, drug toxicity
antigen: IP, intraperitoneal drug administration
antigen: CB, drug combination
antigen: IT, drug interaction
mineral oil: PD, pharmacology
mineral oil: PR, pharmaceutics
mineral oil: DV, drug development
mineral oil: CB, drug combination
mineral oil: IT, drug interaction
aluminum potassium sulfate: PD, pharmacology
aluminum potassium sulfate: PR, pharmaceutics
aluminum potassium sulfate: DV, drug development
aluminum potassium sulfate: CB, drug combination
aluminum potassium sulfate: IT, drug interaction
aluminum hydroxide: PD, pharmacology
aluminum hydroxide: CM, drug comparison
aluminum hydroxide: PR, pharmaceutics
aluminum hydroxide: DV, drug development
aluminum hydroxide: CB, drug combination
aluminum hydroxide: IT, drug interaction
aluminum phosphate: PD, pharmacology
aluminum phosphate: PR, pharmaceutics
aluminum phosphate: DV, drug development
aluminum phosphate: CB, drug combination
aluminum phosphate: IT, drug interaction
saponin: PD, pharmacology
saponin: CM, drug comparison
saponin: PR, pharmaceutics
saponin: DV, drug development
saponin: CB, drug combination
saponin: IT, drug interaction
BCG vaccine: PR, pharmaceutics
BCG vaccine: DV, drug development
BCG vaccine: CB, drug combination
BCG vaccine: IT, drug interaction
recombinant hepatitis B vaccine: PR, pharmaceutics
recombinant hepatitis B vaccine: DV, drug development
recombinant hepatitis B vaccine: CB, drug combination
recombinant hepatitis B vaccine: IT, drug interaction
drug vehicle: PR, pharmaceutics
drug vehicle: PD, pharmacology
drug vehicle: CM, drug comparison
drug vehicle: DV, drug development
drug vehicle: CB, drug combination
drug vehicle: IT, drug interaction
liposome: PR, pharmaceutics
liposome: PD, pharmacology
liposome: IP, intraperitoneal drug administration
liposome: AN, drug analysis
liposome: DV, drug development
liposome: DT, drug therapy
liposome: CB, drug combination
liposome: IT, drug interaction
tetanus toxoid: PR, pharmaceutics
tetanus toxoid: PD, pharmacology
tetanus toxoid: DV, drug development
tetanus toxoid: CB, drug combination
tetanus toxoid: IT, drug interaction
hepatitis A vaccine: DV, drug development
hepatitis A vaccine: DT, drug therapy
hepatitis A vaccine: PR, pharmaceutics
hepatitis A vaccine: IM, intramuscular drug administration
hepatitis A vaccine: CB, drug combination
hepatitis A vaccine: IT, drug interaction
influenza vaccine: DV, drug development
influenza vaccine: DT, drug therapy

influenza vaccine: PR, pharmaceutics
influenza vaccine: IM, intramuscular drug administration
influenza vaccine: CB, drug combination
influenza vaccine: IT, drug interaction
ISCOM: PR, pharmaceutics
ISCOM: DV, drug development
ISCOM: PD, pharmacology
ISCOM: CB, drug combination
ISCOM: IT, drug interaction
Escherichia coli vaccine: DT, drug therapy
Escherichia coli vaccine: DV, drug development
Escherichia coli vaccine: PR, pharmaceutics
Escherichia coli vaccine: PO, oral drug administration
Escherichia coli vaccine: CB, drug combination
Escherichia coli vaccine: IT, drug interaction
Shigella vaccine: DT, drug therapy
Shigella vaccine: DV, drug development
Shigella vaccine: PR, pharmaceutics
Shigella vaccine: PO, oral drug administration
Shigella vaccine: CB, drug combination
Shigella vaccine: IT, drug interaction
diphtheria tetanus vaccine: DT, drug therapy
diphtheria tetanus vaccine: DV, drug development
diphtheria tetanus vaccine: PR, pharmaceutics
diphtheria tetanus vaccine: IM, intramuscular drug administration
diphtheria tetanus vaccine: CB, drug combination
diphtheria tetanus vaccine: IT, drug interaction
amine: PR, pharmaceutics
amine: PD, pharmacology
amine: DV, drug development
amine: CB, drug combination
amine: IT, drug interaction
muramyl dipeptide derivative: PR, pharmaceutics
muramyl dipeptide derivative: PD, pharmacology
muramyl dipeptide derivative: DV, drug development
muramyl dipeptide derivative: AE, adverse drug reaction
muramyl dipeptide derivative: CB, drug combination
muramyl dipeptide derivative: IT, drug interaction
polyglactin: PR, pharmaceutics
polyglactin: PD, pharmacology
polyglactin: DV, drug development
polyglactin: CB, drug combination
polyglactin: IT, drug interaction
drug carrier: PD, pharmacology
drug carrier: DV, drug development
drug carrier: AE, adverse drug reaction
drug carrier: PR, pharmaceutics
drug carrier: CB, drug combination
drug carrier: IT, drug interaction
cytokine: PD, pharmacology
cytokine: DV, drug development
cytokine: AE, adverse drug reaction
cytokine: PR, pharmaceutics
cytokine: CB, drug combination
cytokine: IT, drug interaction
lipopolysaccharide: PD, pharmacology
lipopolysaccharide: PR, pharmaceutics
lipopolysaccharide: AE, adverse drug reaction
lipopolysaccharide: DV, drug development
lipopolysaccharide: CB, drug combination
lipopolysaccharide: IT, drug interaction
endotoxin: PD, pharmacology
endotoxin: PR, pharmaceutics
endotoxin: AE, adverse drug reaction
endotoxin: DV, drug development
endotoxin: CB, drug combination
endotoxin: IT, drug interaction

RN unindexed drug
 RN (protein) 67254-75-5; (aluminum potassium sulfate) 10043-67-1; (aluminum hydroxide) 1330-44-5, 20257-20-9, 21645-51-2, 80206-84-4; (aluminum phosphate) 7784-30-7; (saponin) 8047-15-2; (tetanus toxoid) 57425-69-1, 93384-51-1; (polyglactin) 26780-50-7, 34346-01-5
 CN (1) Epaxal berna
 CO (1) Swiss Serum and Vaccine Institute (Switzerland); Novavax

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 on STN

ACCESSION NUMBER: 86163437 EMBASE
 DOCUMENT NUMBER: 1986163437
 TITLE: Two toxin-converting phages from Escherichia coli O157:H7 strain 933 encode antigenically distinct toxins with similar biologic activities.
 AUTHOR: Strockbine N.A.; Marques L.R.M.; Newland J.W.; et al.
 CORPORATE SOURCE: Department of Microbiology, Uniformed Services University of the Health Sciences, Bethesda, MD 20814-4799, United States
 SOURCE: Infection and Immunity, (1986) 53/1 (135-140).
 CODEN: INFIBR
 COUNTRY: United States
 DOCUMENT TYPE: Journal
 FILE SEGMENT: 004 Microbiology
 052 Toxicology
 LANGUAGE: English

AB Escherichia coli O157:H7 strain 933 contains two distinct toxin-converting phages (933J and 933W). The biologic activities and antigenic relationship between the toxins produced by 933J and 933W lysogens of *E. coli* K-12, as well as the homology of the genes that encode the two toxins, were examined in this study. The 933J and 933W toxins, like Shiga toxin produced by *Shigella dysenteriae* type 1, were cytotoxic for the same cell lines, caused paralysis and death in mice, and caused fluid accumulation in rabbit ileal segments. The cytotoxic activity of 933J toxin for HeLa cells was neutralized by anti-Shiga toxin, whereas the activity of 933W toxin was not neutralized by this antiserum. In contrast, an antiserum prepared against *E. coli* K-12(933W) neutralized 933W toxin but not 933J toxin or Shiga toxin. For *E. coli* 933, most of the cell-associated cytotoxin was neutralized by anti-Shiga toxin, whereas most of the extracellular cytotoxin was neutralized by anti-933W toxin. However, a mixture of these antisera indicated the presence of both toxins in cell lysates and culture supernatants. Among 50 elevated cytotoxin-producing strains of *E. coli*, we identified 11 strains isolated from cases of diarrhea, hemorrhagic colitis, or hemolytic uremic syndrome that produced cell-associated cytotoxins which were neutralized by the 933W antitoxin. Southern hybridization studies showed that the cloned toxin structural genes from phage 933J hybridized with DNA from phage 933W under conditions estimated to allow no more than 26% base-pair mismatch. These findings indicate that *E. coli* produces two genetically related but antigenically distinct cytotoxins with similar biologic activities which we propose to name Shiga-like toxins I and II. Strains of *E. coli* that produce elevated levels of Shiga-like toxin I or Shiga-like toxin II, or both, have been associated with the clinical syndromes of diarrhea, hemorrhagic colitis, and hemolytic uremic syndrome.

CT Medical Descriptors:
 *escherichia coli
 shigella dysenteriae
 priority journal
 etiology
 heredity
 human
 Drug Descriptors:
 *cytotoxin
 *toxin

=> d ibib abs 8

L135 ANSWER 8 OF 13 USPATFULL on STN
 ACCESSION NUMBER: 2002:287161 USPATFULL
 TITLE: Enterohemorrhagic escherichia coli vaccine
 INVENTOR(S): Finlay, Brett, British Columbia, CANADA
 Potter, Andrew A., Saskatchewan, CANADA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002160020	A1	20021031
APPLICATION INFO.:	US 2002-39760	A1	20020103 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-259818P	20010104 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	ROBINS & PASTERNAK LLP, Suite 200, 90 Middlefield Road, Menlo Park, CA, 94025	
NUMBER OF CLAIMS:	34	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	9 Drawing Page(s)	
LINE COUNT:	1485	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
AB Compositions and methods for stimulating an immune response against a secreted enterohemorrhagic Escherichia coli (EHEC) antigen are disclosed. The compositions comprise EHEC cell culture supernatants.		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d ibib abs 9

L135 ANSWER 9 OF 13 USPATFULL on STN
 ACCESSION NUMBER: 2002:280552 USPATFULL
 TITLE: Kyberdrug as autovaccines with immune-regulating effects
 INVENTOR(S): Zimmermann, Kurt, Herborn-Seelbach, GERMANY, FEDERAL REPUBLIC OF
 Paradies, H. Henrich, Iserlohn, GERMANY, FEDERAL REPUBLIC OF
 Rusch, Volker, Herborn, GERMANY, FEDERAL REPUBLIC OF

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002155997	A1	20021024
APPLICATION INFO.:	US 2001-971557	A1	20011005 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-238656P	20001006 (60)
	US 2001-263494P	20010123 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	SCULLY, SCOTT, MUPRHY & PRESSER, 400 Garden City Plaza, Garden City, NY, 11530	
NUMBER OF CLAIMS:	50	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	10 Drawing Page(s)	
LINE COUNT:	3156	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
AB The present invention is directed to a "Kyberdrug" and to a pharmaceutical composition containing an effective amount of the Kyberdrug and a pharmaceutical carrier therefor, and its medicinal use as an immune modulating drug exhibiting autovaccine-like activities.		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic 9

L135 ANSWER 9 OF 13 USPATFULL on STN

- SUMM . . . It plays a role in protecting the cell from cell death and phagocytosis, even though the presence of this O-specific antigen is not necessary for the survival of the bacteria in vitro.
- SUMM . . . carry immunodominant structures (O-factors) against which the host immune system produces antibodies. Therefore, the O-specific chain is responsible for the O-antigenic properties of the lipopolysaccharides. The O-factor has also been found to promote such beneficial effects as suppressing tumor growth by. . .
- SUMM . . . these bacteria exhibit both beneficial and adverse effects. These bacteria, particularly the enterobacteriaceae (e.g., E. Coli), produce compounds which provide immunostimulating effects, but, at the same time, also provide the deleterious and lethal side effects. Thus, the objective was to find. . .
- SUMM . . . biologically active material can be administered as part of a desensitization regimen or as a Type I of a prophylactic vaccine to prevent a Type I hypersensitivity reaction.
- SUMM [0020] U.S. Pat. No. 5,776,468 discloses a novel vaccine composition comprising small particles of 3-O-deacylated monophosphoryl lipid A. In particular, it describes how to prepare a certain particle size of less than 120 nm, which can applied to induce protective immunity, even with very low doses of antigen. The specification provides evidence that these compounds protect against primary and current infections, and stimulate advantageously both specific humoral by neutralizing antibodies, and also effector cell mediated immune response. Moreover, it is alleged that vaccine compositions comprising small particles of the 3-O-deacylated monophosphoryl lipid A molecules, especially those below 120 nm, as measured by photon. . .
- SUMM [0022] The present inventors, through a series of controlled isolation steps, have isolated a biologically active material which contains the immunostimulating effects without the toxic side effects. More specifically, they found a biological material which minimizes or completely eliminates the toxic. . .
- SUMM . . . bacteria of enterobacteriaceae, they were able to isolate a compound and prepare a drug therefrom which makes use of the immunostimulating effects attributable to this class of bacteria and simultaneously substantially eliminate the deleterious lethal side effects due to endotoxin induced. . .
- SUMM . . . factors for AMP adenylate cyclase, or c-GMP Guanylate-cyclase. It, in addition, does not contain the eae gene sequence characteristic for EHEC or EPEC. It does not possess the lipid A molecules described hereinabove, in its toxic form. The bacteria producing the. . .
- DETD . . . and control cellular events which are concerned especially with antagonistic control systems in humans and other mammals. They act like vaccines, but the Kyberdrugs are not vaccines or like substances.
- DETD . . . exhibit antagonistic activities against other bacteria, retroviruses and coated and uncoated viruses, but not against themselves. They possess all the antigenic components for exerting antigenicity, including immune-stimulating effects, without having the deleterious effects of endotoxins mediated bacterial translocation through the gut. Moreover, and most importantly,. . .
- DETD . . . enterocyte and destruction of microvilli are avoided. In addition, the enterobacteriaceae are also devoid of enterotoxigenic E.Coli (ETEC), the entero-invasive E.Coli (EIEC) and the enterohemorrhagic E.Coli (EHEC). . .
- DETD [0105] (k) it does not have the eae gene sequence, characteristic for EHEC and EPEC.

- DETD . . . to protect the human (mammalian) organism against foreign invaders. Particularly, the Kyberdrug are capable of stimulating those cells which produce antigens and can increase these specific antigens in order to delete the invaded hostile microorganism, or chronic inflammation. The fast selection is brought about by the stimulated. . .
- DETD . . . the atopy. Responding in an unique way to the Kyberdrug, the atopy response is reduced through the interaction of the antigen with the Kyberdrug, e.g., thereby reducing swelling from the influx of water and immune cells into tissue, local blood-blood vessel. . .
- DETD [0169] Kyberdrugs may also be incorporated into regular and clinical immunization, also with other injectable vaccines, e.g. diphtheria, pertussis, tetanus;
- DETD . . . to protect the human (mammalian) organism against foreign invaders. Particularly, the Kyberdrugs are capable of stimulating those cells which produce antigens and can increase these specific antigens in order to delete the invaded hostile microorganism or chronic inflammation. The fast selection is brought about by the stimulated. . .
- DETD . . . 0.1 to about 0.5M and most preferably at about 0.1M to about 0.2M, the Kyberdrug can be used as a vaccine against viruses and bacteria, e.g. against Hepatitis B surface antigen. Moreover, the Kyberdrugs can be used as an adjuvant against Type I hypersensitivity to allergens, e.g. pollen allergens, insect saliva. . .
- DETD . . . was added thereto. The solution was turbid; in addition, a microcrystalline precipitate was formed which was filtered off, and the supernatant was concentrated until no more microcrystalline precipitate developed. The combined microcrystalline precipitates were dried over P.sub.40.sub.10 in vacuum at 20.degree.. . .
- DETD . . . and HOO.sup.- anions generated by alveolar macrophages, peripheral blood mononuclear cells, polymorphonuclear leukocytes, and basophils. The Kyberdrug exhibits also sialoprotein-related antigenicity as noticed from in vitro and in vivo studies of patients suffering from cold & rhinitis, respectively, as determined from. . .
- DETD [0275] Furthermore, inherent .alpha.-2-macroglobulin antigenic determinants when stimulated by the Kyberdrug are also responsible for the ability of the Kyberdrug to diminish the survival of. . .
- DETD [0282] Another unexpected effect of the Kyberdrug which has been observed is the inhibitory action in lymphocyte cell cultures which has been infected with the human immunodeficiency viruses type 1 & 2 (HIV 1 & 2) from blood of. . . of the infection was monitored by i.) the amount of HIV particles by quantitatively assaying virion-associated protein directly, e.g. p24 antigen capture or indirectly through the reverse transcriptase activity (RT), and the gp120 glycoprotein; ii.) particle infectivity using TCID₅₀ (tissue culture infectious dose, half-maximal) determinations, and the syncytium formation (SCF) assay. The advantages of using the p24 antigen capture assay, the RT-assay as well as the gp120 protein assay is related to the sensitivity and quantitation possibility in. . . proteins including their concentrations vs. concentration of the Kyberdrug. The RT-assay is known to be less sensitive than the p24 antigen capture assay, but found to be as sensitive as the gp120 assay. The assay systems are those as described in. . .
- DETD . . . exhibited anti-HIV activities represented by low EC₅₀ values ranging from 0.4 to 0.6 .mu.g per mL when administered to the cell cultures in 0.154 M NaCl. pH changes or different ionic strength did not change the EC₅₀ values significantly. Furthermore, the cytotoxicity. . .
- DETD [0289] CTL cell culture
- DETD [0312] EL4/NOB-1 cell culture
- DETD [0322] 5. Remove 50 .mu.l of the supernatant from each well and determine the IL-2 present using the CTL-2 bioassay.sup.c (see Protocol 1). The amount of IL-2 in the supernatants will be proportional to the amount of IL-1 in the original samples. Supernatants from the EL4/NOB-1 cells can be removed and stored

frozen until the IL-2 can be conveniently assayed.

DETD . . . positive
 for cGMP Guanylate-cyclase
 Determination of adhesion negative
 molecules, e.g., ICAM I-III
 Absence of eae gene sequences, positive
 characteristic for EHEC or
 EPEC
 Stability during storage and positive
 effective for shelf-life of
 the col strain in isotonic
 salt solution
 Stability during. . .

CLM What is claimed is:
 . . . enterobacteriaceae belongs to the strain selected from the group consisting of Bacillus, Bacteroides, Brucella, Carnobacterium, Caulobacter, Citrobacter, Clostridium, Corynebacterium, Enterobacter, Escherichia coli, Halobacteria, Klebsiella, Lactobacillus, Lactococcus, Leuconstoc, Listeria, Micrococcus, Mycobacterium, Neisseria, Pasteurella, Pediococcus, Propionibacterium, Proteus, Pseudomonas, Salmonella, Sarzina, Shigella, Serratia, Staphylococcus, Streptococcus, . . .
 27. A vaccine comprising the biological material of claim 1 or 2.

=> d ibib abs 10

L135 ANSWER 10 OF 13 USPATFULL on STN

ACCESSION NUMBER: 1999:78853 USPATFULL
 TITLE: Method of recovering shiga-like toxins and vaccines comprising inactivated shiga-like toxin
 INVENTOR(S): Vanmaele, Rosa, Edmonton, Canada
 Armstrong, Glen D., Edmonton, Canada
 PATENT ASSIGNEE(S): Sybsorb Biotech, Inc., Calgary, Alberta, Canada
 (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5922848		19990713
APPLICATION INFO.:	US 1998-58775		19980413 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1997-866921, filed on 30 May 1997		

DOCUMENT TYPE: Utility
 FILE SEGMENT: Granted
 PRIMARY EXAMINER: Housel, James C.
 ASSISTANT EXAMINER: Graser, Jennifer
 LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis, LLP
 NUMBER OF CLAIMS: 6
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
 LINE COUNT: 1009

CAS INDEXING IS AVAILABLE FOR THIS PATENT..

AB Disclosed are methods of purifying shiga-like toxins (SLTs) from Polymyxin B sulfate extracts of Verotoxin-producing Escherichia coli. The methods are facile, efficient and reproducible. In another aspect, the toxin is inactivated for use in a vaccine against SLT mediated disease conditions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic 10

L135 ANSWER 10 OF 13 USPATFULL on STN

TI Method of recovering shiga-like toxins and vaccines comprising inactivated shiga-like toxin

AB Disclosed are methods of purifying shiga-like toxins (SLTs) from Polymyxin B sulfate extracts of Verotoxin-producing Escherichia coli. The methods are facile, efficient and reproducible. In another aspect, the toxin is inactivated for use in a vaccine against SLT mediated disease conditions.

SUMM In another aspect, the SLTs recovered in this invention are inactivated to provide for an immunoprotective vaccine.

SUMM 11. O'Brien et al., Purification of Shigella Dysenteriae 1 (Shiga)-Like Toxin From Escherichia coli 0157:H7 Strain Associated with Haemorrhagic Colitis, Lancet Sep. 3, 1983, page 573.

SUMM 16 Lemieux, R.U., et al., The properties of a 'synthetic' antigen related to the blood-group Lewis A, J. Am. Chem. Soc., 97:4076-83 (1975).

SUMM 21 Paulsen, H., Synthese von oligosaccharid-determination mit amid-spacer vom typ des T-antigens, Carbohydr. Res., 104:195-219 (1982).

SUMM 22 Chernyak, A. Y., et al., A New Type of Carbohydrate-Containing Synthetic Antigen: Synthesis of Carbohydrate-Containing Polyacrylamide Copolymers having the Specificity of 0:3 and 0:4 Factors of Salmonella, Carbohydrate Research, 128:269-282 (1984).

SUMM 26 Lemieux, R. U., et al., Artificial Oligosaccharide Antigenic Determinants, U.S. Pat. No. 4,238,473, issued Dec. 9, 1980.

SUMM . . . et al., Synthesis of space arm, lipid, and ethyl glycosides of the trisaccharide portion [.alpha.-D-Gal-(1-4)-g-DGal(1-4)-O-D-Glc] of the blood group p.sup.k antigen: preparation of neoglycoproteins, Carbohydrate Research, 127: 15-25 (1984).

SUMM 30 Rappuoli, R., Toxin Inactivation and Antigen Stabilization: Two Different Uses of Formaldehyde, Vaccine, 12:579-581 (1994).

SUMM Different antigenically distinct SLTs have been described including SLT-I and SLT-II. SLT-I is nearly identical to Shiga toxin. SLT-II, including known variants. . .

SUMM . . . the 0157:H7 E. coli serotype is isolated from 95% of cases of SLT mediated infections whereas, in other locations, different enterohemorrhagic E. coli serotypes predominate. Serotype 0157:H7 E. coli can readily be identified in the clinical laboratory because of its inability to utilize. . . non-0157:H7 serotypes predominate. Accordingly, clinical diagnosis of SLT mediated infections in a patient by assaying only for the presence of enterohemorrhagic 0157:H7 E. coli serotypes is not advised.

SUMM Another diagnostic method is the detection of SLTs in the stools of patients suspected of being infected with enterohemorrhagic E. coli. Diagnostic kits used in the detection of SLTs are now commercially available but, nevertheless, these tests require a purified source. . .

SUMM . . . for patients, particularly patients with weakened immune systems, wherein inactivated forms of the SLTs could be used as an immunoprotective vaccine.

SUMM Specifically, enterohemorrhagic E. coli infections are treated clinically as self-limiting because antibiotics are of little therapeutic value. The failure of antibiotic therapy may relate. . .

SUMM . . . to provide protection. Accordingly, any person with a compromised immune system could suffer a lethal infection upon first exposure to enterohemorrhagic E. coli infection if their immune system was not primed. One method for so priming such persons would be to administer an immunoprotective vaccine to that person which vaccine would prophylactically act to prevent the occurrence of this disease.

SUMM Such vaccines would, of course, require purification of SLTs which are subsequently inactivated. Various methods have been heretofore disclosed for isolating SLTs. . . however, are in one manner or another not preferred for preparing large quantities of purified SLTs for use in a vaccine. For example, receptor analog affinity

- chromatography with a glycoprotein present in hydatid cyst fluid has been utilized.^{4,7,10,13} This glycoprotein possesses . . . glycolipid. However, safety concerns regarding possible contamination of the isolated SLTs would preclude the use of these recovered SLTs in vaccine preparations.
- SUMM . . . SLTs by small amounts of Gb._{sub.3} is possible and such contamination would preclude its use in the preparation of a vaccine.
- SUMM . . . For example, guanidine HCl^{3,6}, 10% SDS in boiling water², MgCl_{sub.2}^{4,7,8,10,12} all have been used. The protein thus recovered may lose antigenic epitopes, be less immunogenic and, consequently, provide an inferior vaccine.
- SUMM . . . is apparent that a need for a rapid, inexpensive method of recovering shiga-like toxins is desirable. Further, a safe, immunoprotective vaccine is desirable.
- SUMM . . . utilize any glycoconjugate to effect recovery of the SLT eliminating possible contamination and safety concerns in the preparation of the vaccine.
- SUMM In a composition aspect, this invention is directed to inactivated SLTs which are useful as vaccines. Accordingly, in this aspect, this invention is directed to an immunoprotective vaccine against SLT mediated disease conditions which vaccine comprises an immunoprotective amount of inactivated SLT and a pharmaceutically acceptable carrier.
- DETD . . . elution recovery step. The methods provide an economical supply of SLTs for use, e.g., in the preparation of an immunoprotective vaccine.
- DETD The term "shiga-like toxins" or "SLT" as used herein refers to a group of toxins produced by *enterohemorrhagic E. coli* that resemble the *Shigella*-produced shiga toxins as commonly understood in the art. Such SLTs include Shiga-like toxin I and Shiga-like. . .
- DETD . . . used herein means an aqueous or organic solution comprising SLTs such as, for example, growth media from the culture of *enterohemorrhagic E. coli* and the like.
- DETD . . . by the ability to elicit significant levels of IgG and opsonic activity. An immunological memory is developed to the immunogenic antigen such that the antibodies produced ameliorate the infection and disease condition mediated by the pathogen.
- DETD . . . challenge with an active SLT the human or animal is unaffected. The inactivated toxin is suitable for use in a vaccine directed against SLT mediated disease conditions. Alternatively, the inactivated toxin may serve as a carrier protein for weakly immunogenic antigens.
- DETD "Hapten" means an antigen, including an incomplete or partial antigen which may not be capable, alone, of causing the production of antibodies. A hapten may elicit a T cell independent. . .
- DETD . . . Preferably the liquid sample is centrifuged at a sufficient speed and for an appropriate time to pellet cellular debris. The supernatant or fraction containing the toxin is used in the next step.
- DETD . . . -70.degree. C. Additionally, the recovered toxin may be lyophilized to form a powder for pharmaceutical use in, for example, a vaccine.
- DETD The recovered toxins, prepared as above, are suitable for use in an immunoprotective vaccine once they have been inactivated. The toxins may be inactivated by any means known in the art. Such methods include. . . alkali metal salts of oxymethane sulfenic acid, protease treatment in the presence of sulfhydryl reducing agents and the like. See Vaccine Preparation Techniques, edited by J. I. Duffy, 1980. A preferred method is formaldehyde treatment of the toxin.
- DETD . . . deactivating agent chosen such that the toxin retains immunogenic epitopes but lacks toxicity. The deactivation techniques to arrive at immunoprotective vaccines are well within the skill of the art and, include variations in, for example, the concentration of the deactivating agent,. . .

DETD . . . remove the deactivating agent and filtered through a suitable sterilizing filter, thus providing sterile, detoxified SLT useful as a fluid vaccine. The fluid vaccine may be lyophilized to form a powder useful in the formulation of a pharmaceutical composition. Such pharmaceutical compositions may be. . .

DETD An adjuvant may optionally be added to the thus obtained fluid or solid vaccine. An adjuvant is any substance whose admixture with the detoxified SLT increases the immunological response. Such adjuvants are well known. . .

DETD The SLT vaccine may be administered intraperitoneally, intramuscularly, orally and the like. For oral administration, the fluid vaccine is preferably given with an appropriate antacid buffer to protect against digestion in the stomach. Alternatively, the sterile, detoxified SLT. . . a protein with lectin or lectin-like binding activity to glycoproteins or glycolipids in the intestinal mucosa or co-administered as an immunostimulating complex and the like for vaccine administration.

DETD . . . The prepared microparticles are taken up by the Peyer's patches of the gut-associated lymph tissue, then phagocytosed by macrophages. Oral vaccine administration advantageously induces both secretory and systemic immunoprotection.

DETD The detoxified toxin may be used in a vaccine directed to enterohemorrhagic *E. coli* SLTs and associated disease conditions. Alternatively, the inactivated toxin may be used as a carrier protein for haptens and T-cell independent antigens. Such a carrier protein simulates an immunoprotective response to a hapten and converts a T-cell independent antigen into a T-cell dependent antigen.

DETD The dosage of the vaccine necessary is readily determined by the attending clinician in view of the weight, age, physical condition and the like of. . .

DETD . . . g at 4.degree. C. to sediment bacterial cell debris. Next, SYNSORB-P1 disaccharide (15 gram/L) was added to the cell-free culture supernatant solution and the resulting mixture was incubated, with vigorous shaking, for 30 minutes at room temperature. The SYNSORB-P1 disaccharide was. . .

DETD Vaccine Preparation

DETD . . . inactivated toxin is dialyzed against phosphate buffered saline (PBS) and sterile filtered to yield a fluid preparation useful as a vaccine.

CLM What is claimed is:

1. A method for making an immunoprotective vaccine against SLT mediated disease conditions comprising: (a) purifying SLT from a sample containing said SLT which purifying method comprises: i). . .
4. A method of making an immunoprotective vaccine against SLT mediated disease conditions which method comprises combining an immunoprotective effective amount of purified inactivated SLT essentially free of. . .

=> d ibib abs hitrn 11

L135 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1
 ACCESSION NUMBER: 2002:521530 HCAPLUS
 DOCUMENT NUMBER: 137:92729
 TITLE: Vaccine compositions comprising
 enterohemorrhagic *Escherichia*
 coli antigen and immune adjuvant
 INVENTOR(S): Finlay, Brett; Potter, Andrew A.
 PATENT ASSIGNEE(S): University of Saskatchewan, Can.; University of
 British Columbia
 SOURCE: PCT Int. Appl., 53 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053181	A1	20020711	WO 2002-CA19	20020103
WO 2002053181	C1	20020919		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002160020	A1	20021031	US 2002-39760	20020103
EP 1349570	A1	20031008	EP 2002-726978	20020103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.: US 2001-259818P P 20010104				
WO 2002-CA19 W 20020103				
AB	Compns. and methods for stimulating an immune response against a secreted enterohemorrhagic <i>Escherichia coli</i> (EHEC) antigen are disclosed. The compns. comprise EHEC cell culture supernatants contg. antigen selected from EspA, EspB, EspD, Tir and Intimin. The immune adjuvant is an oil-in-water emulsion comprising mineral oil and dimethyldioctadecylammonium bromide, or VSA3.			
IT	3700-67-2, Dimethyldioctadecylammonium bromide RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (vaccine compns. comprising nucleic acid-based or recombinant proteins of enterohemorrhagic <i>Escherichia coli</i> EspA, EspB, EspD, Tir, and/or Intimin and adjuvant)			
REFERENCE COUNT:	5	THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

=> d ibib abs hitrn 12

L135 ANSWER 12 OF 13 HCPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2001:512570 HCPLUS
 DOCUMENT NUMBER: 135:226057
 TITLE: Interaction between emulsion droplets and *Escherichia coli* cells
 AUTHOR(S): Li, J.; McClements, D. J.; McLandsborough, L. A.
 CORPORATE SOURCE: Molecular Circuitry Inc., King of Prussia, PA, 19406, USA
 SOURCE: Journal of Food Science (2001), 66(4), 570-574
 CODEN: JFDSAZ; ISSN: 0022-1147
 PUBLISHER: Institute of Food Technologists
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Oil-in-water emulsions (20% n-hexadecane, vol./vol.) were stabilized by dodecyltrimethylammonium bromide (DTAB), Tween 20, or SDS. Particle size distribution and creaming stability were measured before and after adding *Escherichia coli* cells to emulsions. Both *E. coli* strains promoted droplet flocculation, coalescence, and creaming in DTAB emulsions, although JM109 cells (surface charge = -35 mV) caused faster creaming than E21 cells (surface charge = -5 mV). Addn. of bacterial cells to SDS emulsions promoted some flocculation and coalescence, but creaming stability was unaffected. Droplet aggregation and accelerated creaming were not obsd. in emulsions prep'd. with Tween 20. Surface charges of bacterial cells and emulsion droplets played a key role in emulsion stability.
 REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ind 12

L135 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
 CC 17-2 (Food and Feed Chemistry)
 ST emulsion Escherichia surface charge creaming
 IT Escherichia coli
 (O157:H7; emulsion droplets interaction with
 Escherichia coli cells)
 IT Surface electric charge
 (biol.; emulsion droplets interaction with Escherichia coli cells)
 IT Coalescence
 Escherichia coli
 Flocculation
 Particle size distribution
 (emulsion droplets interaction with Escherichia coli cells)
 IT Food functional properties
 (emulsion stability; emulsion droplets interaction with Escherichia
 coli cells)
 IT Emulsions
 (oil-in-water; emulsion droplets interaction with Escherichia coli
 cells)
 IT 151-21-3, Sodium dodecyl sulfate, biological studies 1119-94-4,
 Dodecyltrimethylammonium bromide 9005-64-5, Tween 20
 RL: BUU (Biological use, unclassified); PEP (Physical, engineering or
 chemical process); BIOL (Biological study); PROC (Process); USES (Uses)
 (emulsion droplets interaction with Escherichia coli cells)

=> d ibib abs hitrn 13

L135 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2000:190092 HCAPLUS
 DOCUMENT NUMBER: 132:346363
 TITLE: Oral immunization of mice with a
 glycoconjugate vaccine containing
 the O157 antigen of Escherichia coli
 O157:H7 admixed with cholera toxin
 fails to elicit protection against subsequent
 colonization by the pathogen
 AUTHOR(S): Conlan, J. Wayne; Kuolee, Rhonda; Webb, Ann; Cox,
 Andrew D.; Perry, Malcolm B.
 CORPORATE SOURCE: Institute for Biological Sciences, National Research
 Council Canada, Ottawa, ON, K1A 0R6, Can.
 SOURCE: Canadian Journal of Microbiology (2000), 46(3),
 283-290
 CODEN: CJMIAZ; ISSN: 0008-4166
 PUBLISHER: National Research Council of Canada
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB It has been postulated that a humoral immune response directed against the
 O157 antigen of Escherichia coli O157:
 H7, and expressed in the intestine, might afford protection from
 colonization and consequent infection by this enteric pathogen. The
 present study was conducted to det. whether such an immune response can be
 exptl. generated in mice. To this end, mice were orally immunized with a
 glycoconjugate vaccine consisting of horse serum albumin and the O157
 polysaccharide admixed with the mucosal adjuvant, cholera toxin.
 Mice consistently developed robust local and systemic immune responses to
 the cholera toxin adjuvant, but were far from uniformly reactive
 to the test vaccine. Moreover, vaccinated mice were as susceptible to
 transient intestinal colonization following challenge with an isolate of
 E. coli O157:H7 as unvaccinated control mice. These
 results indicate that this vaccination approach is unlikely to be
 straightforward in target bovine or human hosts.
 REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ind 13

L135 ANSWER 13 OF 13 HCPLUS COPYRIGHT 2003 ACS on STN
CC 15-2 (Immunochemistry)
ST oral vaccine O antigen Escherichia
IT Toxins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cholera; immunization with glycoconjugate vaccine contg.
O-antigen of *Escherichia coli* 0157:
H7 admixed with cholera toxin fails to elicit protection against subsequent colonization)
IT O antigen
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(conjugates, with serum albumin; immunization with glycoconjugate vaccine contg. O-antigen of *Escherichia coli* 0157:H7 admixed with cholera toxin fails to elicit protection against subsequent colonization)
IT *Escherichia coli*
(immunization with glycoconjugate vaccine contg. O-antigen of *Escherichia coli* 0157:H7 admixed with cholera toxin fails to elicit protection against subsequent colonization)
IT Intestine
(immunization with glycoconjugate vaccine contg. O-antigen of *Escherichia coli* 0157:H7 admixed with cholera toxin fails to elicit protection against subsequent colonization of)
IT Vaccines
(oral; immunization with glycoconjugate vaccine contg. O-antigen of *Escherichia coli* 0157:
H7 admixed with cholera toxin fails to elicit protection against subsequent colonization)
IT Albumins, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(serum, conjugates, with O-antigens; immunization with glycoconjugate vaccine contg. O-antigen of *Escherichia coli* 0157:H7 admixed with cholera toxin fails to elicit protection against subsequent colonization)

Hit List

Search Results - Record(s) 1 through 10 of 13 returned.

1. Document ID: US 20020160020 A1

Using default format because multiple data bases are involved.

L1: Entry 1 of 13

File: PGPB

Oct 31, 2002

PGPUB-DOCUMENT-NUMBER: 20020160020

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020160020 A1

TITLE: Enterohemorrhagic escherichia coli vaccine

PUBLICATION-DATE: October 31, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Finlay, Brett	British Columbia		CA	
Potter, Andrew A.	Saskatchewan		CA	

US-CL-CURRENT: 424/257.1; 435/252.33

-
2. Document ID: US 6572833 B1

L1: Entry 2 of 13

File: USPT

Jun 3, 2003

US-PAT-NO: 6572833

DOCUMENT-IDENTIFIER: US 6572833 B1

TITLE: Ammonium nitrate bodies and a process for their production

DATE-ISSUED: June 3, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE ZIP CODE	COUNTRY
Cooper; John	Ayr, KA7 4DE		GB
Brues; Michael	Kirkland, Quebec	H9J 2N9	CA
Hsu; Noel	Aurora	CO 80013	
Peddie; Ronald O.	Warners Bay, New South Wales, 2282		AU

US-CL-CURRENT: 423/266; 149/46, 23/300, 23/302A, 423/396

3. Document ID: US 6539274 B1

L1: Entry 3 of 13

File: USPT

Mar 25, 2003

US-PAT-NO: 6539274

DOCUMENT-IDENTIFIER: US 6539274 B1

** See image for Certificate of Correction **

TITLE: Method for compensating for temperature-related dimensional deviations in machine geometry

DATE-ISSUED: March 25, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rauth; Michael	Traunreut			DE
<u>Zacek; Johann</u>	Evenhausen			DE

US-CL-CURRENT: 700/159; 409/238, 700/193[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Dependencies](#) [Annotations](#) [Claims](#) [KOMC](#) [Drawn De](#) 4. Document ID: US 6177682 B1

L1: Entry 4 of 13

File: USPT

Jan 23, 2001

US-PAT-NO: 6177682

DOCUMENT-IDENTIFIER: US 6177682 B1

TITLE: Inspection of ball grid arrays (BGA) by using shadow images of the solder balls

DATE-ISSUED: January 23, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bartulovic; Vuk	Beaconsfield			CA
Lucic; Miljenko	Lachine			CA
<u>Zacek; Gabriele</u>	Montreal			CA

US-CL-CURRENT: 250/559.44; 250/559.12, 356/237.4, 382/150[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Dependencies](#) [Annotations](#) [Claims](#) [KOMC](#) [Drawn De](#) 5. Document ID: US 5719100 A

L1: Entry 5 of 13

File: USPT

Feb 17, 1998

US-PAT-NO: 5719100

DOCUMENT-IDENTIFIER: US 5719100 A

TITLE: Water treatment compositions

DATE-ISSUED: February 17, 1998

h e b b g e e e f e c e ef b e

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Zahradnik; Rudolf	Prague 7			CS
Barber; Bruce	Duxbury	MA	02332	

US-CL-CURRENT: 502/417; 210/501, 210/502.1, 252/187.23

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Searches](#) | [Attachments](#) | [Claims](#) | [KWMC](#) | [Draw De](#)

 6. Document ID: US 5409044 A

L1: Entry 6 of 13

File: USPT

Apr 25, 1995

US-PAT-NO: 5409044

DOCUMENT-IDENTIFIER: US 5409044 A

TITLE: Circular loom having improved shuttle retention

DATE-ISSUED: April 25, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lin; Yao-Chang	401 Tung Dist., Taichung City			TW

US-CL-CURRENT: 139/457

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Searches](#) | [Attachments](#) | [Claims](#) | [KWMC](#) | [Draw De](#)

 7. Document ID: US 5284540 A

L1: Entry 7 of 13

File: USPT

Feb 8, 1994

US-PAT-NO: 5284540

DOCUMENT-IDENTIFIER: US 5284540 A

TITLE: Method of making laminates from polyethylene foils and the like

DATE-ISSUED: February 8, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Roth; Roland	Teningen-Nimburg			DE
Schick; Henning	Heitersheim			DE
Bloo; Johann	Seewalchen			AT
<u>Zacek; Franz</u>	Vocklabruck			AT

US-CL-CURRENT: 156/160; 156/161, 156/163, 156/164, 156/229, 428/515

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Searches](#) | [Attachments](#) | [Claims](#) | [KWMC](#) | [Draw De](#)

 8. Document ID: US 5266808 A

h e b b g e e e f e c e ef b e

L1: Entry 8 of 13

File: USPT

Nov 30, 1993

US-PAT-NO: 5266808

DOCUMENT-IDENTIFIER: US 5266808 A

TITLE: Particle detector and method using a helical array of scintillators

DATE-ISSUED: November 30, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Siegmund; Walter P.	Windham	CT		
Nass; Peter	Mainz			DE

US-CL-CURRENT: 250/368; 250/364, 250/367[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Drawn De](#) 9. Document ID: US 4821778 A

L1: Entry 9 of 13

File: USPT

Apr 18, 1989

US-PAT-NO: 4821778

DOCUMENT-IDENTIFIER: US 4821778 A

**** See image for Certificate of Correction ****

TITLE: Circular loom

DATE-ISSUED: April 18, 1989

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Zacek; Franz	Vocklabruck			AT

US-CL-CURRENT: 139/457; 139/459[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KMC](#) | [Drawn De](#) 10. Document ID: US 4778561 A

L1: Entry 10 of 13

File: USPT

Oct 18, 1988

US-PAT-NO: 4778561

DOCUMENT-IDENTIFIER: US 4778561 A

TITLE: Electron cyclotron resonance plasma source

DATE-ISSUED: October 18, 1988

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ghanbari; Ebrahim	Huntington	NY		

h e b b g e e e f e c e ef b e

US-CL-CURRENT: 216/70, 118/50.1, 118/623, 118/728, 156/345.37, 156/345.42,
204/192.1, 204/298.38, 250/423R, 250/424, 427/571, 427/575

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequencies](#) | [Attachments](#) | [Claims](#) | [RIVIC](#) | [Drawn De](#)

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L1: Entry 1 of 13

File: PGPB

Oct 31, 2002

DOCUMENT-IDENTIFIER: US 20020160020 A1

TITLE: Enterohemorrhagic escherichia coli vaccine

Summary of Invention Paragraph:

[0006] Because of the bulk processing of slaughtered cattle and the low number of EHEC O157:H7 (10-100) necessary to infect a human, EHEC O157:H7 colonization of healthy cattle remains a serious health problem. To address this problem, research has focused on improved methods for detecting and subsequently killing EHEC O157:H7 at slaughter, altering the diet of cattle to reduce the number of intestinal EHEC O157:H7 and immunizing animals to prevent EHEC O157:H7 colonization (Zacek D. Animal Health and Veterinary Vaccines, Alberta Research Counsel, Edmonton, Canada, 1997). Recently, the recombinant production and use of EHEC O157:H7 proteins including recombinant EspA (International Publication No. WO 97/40063), recombinant TIR (International Publication No. WO 99/24576), recombinant EspB and recombinant Initimin (Li et al., Infec. Immun. (2000) 68:5090-5095) have been described. However, production and purification of recombinant proteins in amounts sufficient for use as antigens is both difficult and expensive. At the present time, there is no effective method for blocking EHEC O157:H7 colonization of cattle and other mammals and, thereby, for reducing shedding of EHEC into the environment.

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L1: Entry 1 of 13

File: PGPB

Oct 31, 2002

PGPUB-DOCUMENT-NUMBER: 20020160020

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020160020 A1

TITLE: Enterohemorrhagic escherichia coli vaccine

PUBLICATION-DATE: October 31, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Finlay, Brett	British Columbia		CA	
Potter, Andrew A.	Saskatchewan		CA	

APPL-NO: 10/ 039760 [PALM]

DATE FILED: January 3, 2002

RELATED-US-APPL-DATA:

Application is a non-provisional-of-provisional application 60/259818, filed January 4, 2001,

INT-CL: [07] A61 K 39/108, C12 N 1/20

US-CL-PUBLISHED: 424/257.1; 435/252.33

US-CL-CURRENT: 424/257.1; 435/252.33

REPRESENTATIVE-FIGURES: NONE

ABSTRACT:

Compositions and methods for stimulating an immune response against a secreted enterohemorrhagic Escherichia coli (EHEC) antigen are disclosed. The compositions comprise EHEC cell culture supernatants.

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims the benefit under 35 USC .sctn.119(e)(1) of provisional patent application serial no. 60/259,818, filed Jan. 4, 2001, which application is incorporated herein by reference in its entirety.

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S1 12 (ANIMAL (N) HEALTH (2N) VETERINARY? (2N) VACCINE?) (100N) -
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1/3,KWIC/10 (Item 1 from file: 349)
DIALOG(R) File 349:PCT FULLTEXT
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00919430 **Image available**
ENTEROHEMORRAGIC ESCHERICHIA COLI VACCINE
VACCIN CONTRE L'INFECTION PAR LA BACTERIE ESCHERICHIA COLI
ENTEROHEMORRAGIQUE

Patent Applicant/Assignee:
UNIVERSITY OF SASKATCHEWAN, 120 Veterinary Road, Saskatoon, Saskatchewan S7N 5E3, CA, CA (Residence), CA (Nationality), (For all designated states except: US)
UNIVERSITY OF BRITISH COLUMBIA, 2222 Health Sciences Mall, Vancouver, British Columbia V6T 1Z3, CA, CA (Residence), CA (Nationality), (For all designated states except: US)

Patent Applicant/Inventor:
FINLAY Brett, 8491 Seafair Drive, Richmond, British Columbia V7C 1X7, CA, CA (Residence), CA (Nationality), (Designated only for: US)
POTTER Andrew A, 521 Dalhousie Cres., Saskatoon, Saskatchewan S7H 3S5, CA, CA (Residence), CA (Nationality), (Designated only for: US)

Legal Representative:
ERRATT Judy A (et al) (agent), Gowling Lafleur Henderson LLP, Suite 2600, 160 Elgin Street, Ottawa, Ontario K1P 1C3, CA,

Patent and Priority Information (Country, Number, Date):
Patent: WO 200253181 A1 20020711 (WO 0253181)
Application: WO 2002CA19 20020103 (PCT/WO CA0200019)
Priority Application: US 2001259818 20010104

Designated States:
(Protection type is "patent" unless otherwise stated - for applications prior to 2004)
AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
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(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English
Fulltext Word Count: 13723

Fulltext Availability:
Detailed Description

Detailed Description

... intestinal EHEC 0157:H7 and immunizing animals to prevent EHEC 0157:H7 colonization (Zacek D. **Animal Health and Veterinary Vaccines**, Alberta Research Counsel, Edmonton, Canada, 1997). Recently, the recombinant production and use of EHEC 0157:H7 proteins including recombinant EspA...

1/3,KWIC/12 (Item 1 from file: 654)

DIALOG(R)File 654:US Pat.Full.

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0005105263 **IMAGE Available

Derwent Accession: 2002-557723

Enterohemorrhagic escherichia coli vaccine

Inventor: Brett Finlay, INV

Andrew Potter, INV

Correspondence Address: ROBINS & PASTERNAK LLP Suite 200, 90 Middlefield Road, Menlo Park, CA, 94025, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20020160020	A1	20021031	US 200239760	20020103
Provisional	.			US 60-259818	20010104

Fulltext Word Count: 14714

Summary of the Invention:

...intestinal EHEC 0157:H7 and immunizing animals to prevent EHEC 0157:H7 colonization (Zacek D. **Animal Health and Veterinary Vaccines**, Alberta Research Counsel, Edmonton, Canada, 1997). Recently, the recombinant production and use of EHEC 0157:H7 proteins including recombinant EspA...

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L2: Entry 1 of 1

File: PGPB

Oct 31, 2002

PGPUB-DOCUMENT-NUMBER: 20020160020

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020160020 A1

TITLE: Enterohemorrhagic escherichia coli vaccine

PUBLICATION-DATE: October 31, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Finlay, Brett	British Columbia		CA	
Potter, Andrew A.	Saskatchewan		CA	

APPL-NO: 10/ 039760 [PALM]

DATE FILED: January 3, 2002

RELATED-US-APPL-DATA:

Application is a non-provisional-of-provisional application 60/259818, filed January 4, 2001,

INT-CL: [07] A61 K 39/108, C12 N 1/20

US-CL-PUBLISHED: 424/257.1; 435/252.33

US-CL-CURRENT: 424/257.1; 435/252.33

REPRESENTATIVE-FIGURES: NONE

ABSTRACT:

Compositions and methods for stimulating an immune response against a secreted enterohemorrhagic Escherichia coli (EHEC) antigen are disclosed. The compositions comprise EHEC cell culture supernatants.

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims the benefit under 35 USC .sctn.119(e)(1) of provisional patent application serial no. 60/259,818, filed Jan. 4, 2001, which application is incorporated herein by reference in its entirety.

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-
1. [20030166841](#). 24 Jan 01. 04 Sep 03. ESCHERICHIA COLI SECRETED PROTEIN B. Kaper, James B., et al. 530/350; C12P019/12 C07K001/00 C07K014/00 C07K017/00.
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2. [20030143558](#). 28 May 02. 31 Jul 03. Methods for attenuation of virulence in bacteria. Mitchell, Wayne, et al. 435/6; 702/20 C12Q001/68 G06F019/00 G01N033/48 G01N033/50.
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3. [20020160020](#). 03 Jan 02. 31 Oct 02. Enterohemorrhagic escherichia coli vaccine. Finlay, Brett, et al. 424/257.1; 435/252.33 A61K039/108 C12N001/20.
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4. [20020115829](#). 28 Sep 01. 22 Aug 02. Pathogenic escherichia coli associated protein. Finlay, B. Brett, et al. 530/350; A61K039/02 C07K001/00 C07K014/00 C07K017/00.
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5. [6635259](#). 24 Jan 01; 21 Oct 03. Escherichia coli secreted protein B. Kaper; James B., et al. 424/241.1; 424/185.1 424/190.1 435/6 435/7.1 435/7.2 435/7.32 435/7.37 530/350 530/402. A61K039/08.
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6. [6355254](#). 10 Aug 99; 12 Mar 02. Pathogenic Escherichia coli associated protein EspA. Finlay; B. Brett, et al. 424/241.1; 424/185.1 424/190.1 530/350. A61K039/108.
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7. [6291435](#). 01 Mar 00; 18 Sep 01. Treatment of diarrhea caused by enteropathogenic Escherichia coli. Yanmaele; Rosa P., et al. 514/25; 514/53 514/867 536/17.2 536/55.1 536/55.2. A61K031/70.
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8. [6204004](#). 21 Mar 97; 20 Mar 01. Immunodiagnostic test for enterohemorrhagic Escherichia coli infection. Kaper; James B., et al. 435/7.37; 435/6 435/7.32 530/402 536/23.1. G01N033/569.
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9. [WO009740063A2](#). 23 Apr 97. 30 Oct 97. PATHOGENIC ESCHERICHIA COLI ASSOCIATED PROTEIN. FINLAY, B BRETT, et al. C07K001/00;.
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10. [US20030166841A](#). New purified protein called EspB or EspA isolated from enterohemorrhagic Escherichia coli (EHEC), useful for diagnosing whether a subject has been infected with EHEC. JARVIS, K, et al. A61K039/08 C07K001/00 C07K014/00 C07K017/00 C12P019/12.
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L1 and EspA	13

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First Hit

L3: Entry 4 of 13

File: PGPB

Aug 22, 2002

PGPUB-DOCUMENT-NUMBER: 20020115829

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020115829 A1

TITLE: Pathogenic escherichia coli associated protein

PUBLICATION-DATE: August 22, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Finlay, B. Brett	Richmond	MD	CA	
Kenny, Brendan	Bristol	OH	GB	
Stein, Markus	Quercegrossa		IT	
Donnenberg, Michael S.	Baltimore		US	
Lai, Li-Ching	Upper Arlington		US	

US-CL-CURRENT: 530/350

CLAIMS:

We claim:

1. An isolated EspA polypeptide characterized by: a) being a secreted protein from enteropathogenic or enterohemorrhagic E. coli; and b) comprising an amino acid sequence as set forth in SEQ ID NO:2 or SEQ ID NO:4.
- 2.. An isolated polynucleotide encoding the polypeptide of claim 1.
3. An isolated polynucleotide selected from the group consisting of: a) the nucleic acid sequence set forth in SEQ ID NO: 1; b) the nucleic acid sequence set forth in SEQ ID NO: 1, wherein T is U; c) nucleic acid sequences complementary to a); and d) fragments of a), b) or c) that are at least 15 nucleotide bases in length and that hybridize under stringent conditions to DNA which encodes the polypeptide set forth in SEQ ID NO: 2.
4. An isolated polynucleotide selected from the group consisting of: a) the nucleic acid sequence set forth in SEQ ID NO: 3; b) the nucleic acid sequence set forth in SEQ ID NO: 3, wherein T is U; c) nucleic acid sequences complementary to a); and d) fragments of a), b) or c) that are at least 15 nucleotide bases in length and that hybridize under stringent conditions to DNA which encodes the polypeptide set forth in SEQ ID NO: 4.
5. A nucleic acid expression vector comprising a promoter operably linked to the polynucleotide of claim 2.
6. A host cell containing the vector of claim 5.
7. An antibody specific for the polypeptide of claim 1.

8. The antibody of claim 7, wherein the antibody is monoclonal.
9. The antibody of claim 7, wherein the antibody is polyclonal.
10. A method for detecting EspA polypeptide in a sample, comprising: a) contacting the sample with the antibody of claim 7; and b) detecting binding of the antibody of claim 7 to EspA polypeptide, wherein binding is indicative of the presence of EspA polypeptide in the sample.
11. The method of claim 10, wherein the sample is tissue.
12. The method of claim 10, wherein the sample is a biological fluid.
13. The method of claim 10, wherein the presence of EspA polypeptide in the sample is indicative of infection by enteropathogenic E. coli.
14. The method of claim 10, wherein the presence of EspA polypeptide in the sample is indicative of infection by enterohemorrhagic E. coli.
15. A method of immunizing a host susceptible to disease caused by an EspA-producing organism, comprising: a) administering to the host an EspA polypeptide of claim 1; and b) inducing a protective immune response to EspA in the host.
16. The method of claim 15, wherein the EspA-producing organism is E. coli.
17. The method of claim 16, wherein the EspA-producing E. coli. is enteropathogenic E. coli.
18. The method of claim 16, wherein the EspA-producing E. coli. is enterohemorrhagic E. coli.
19. A method of ameliorating disease caused by EspA-producing organism, comprising: a) immunizing a host with the polypeptide of claim 1; and b) inducing an immune response in the host to the EspA polypeptide, thereby ameliorating disease caused by infection of the host by EspA-producing organism.
20. The method of claim 19, wherein the EspA-producing organism is E. coli.
21. The method of claim 19, wherein the EspA-producing E. coli. is enteropathogenic E. coli.
22. The method of claim 19, wherein the EspA-producing E. coli. is enterohemorrhagic E. coli.
23. A method for detecting a polynucleotide in a sample, comprising: a) contacting a sample suspected of containing espA polynucleotide with a nucleic acid probe that hybridizes to the polynucleotide of claim 2; and b) detecting hybridization of the probe with the polynucleotide, wherein the detection of hybridization is indicative of espA polynucleotide in the sample.
24. A method for producing a recombinant espA polynucleotide, comprising: inserting a nucleic acid encoding a selectable marker into the polynucleotide of claim 2, such that the resulting polynucleotide encodes a recombinant EspA polypeptide containing the selectable marker.

25. A polynucleotide produced by the method of claim 24.
26. A host cell containing the polynucleotide of claim 25.
27. A method for producing a recombinant EspA polypeptide, comprising: a) growing a host cell containing a polynucleotide encoding a EspA polypeptide of claim 1 under conditions which allow expression of EspA polypeptide; and b) isolating the polypeptide.
28. A method to identify a compound that affects bacterial type III secretion, comprising: a) introducing the polynucleotide of claim 5 into bacteria having a bacterial type III secretion system; b) growing the bacteria under conditions which allow expression of the polypeptide encoded by the polynucleotide; c) contacting the bacteria with a candidate compound; and d) measuring secretion of the polypeptide, and thereby identifying a compound that affects type III secretion.
29. A method for producing a nonpathogenic organism, comprising: a) generating a mutation in a polynucleotide encoding a EspA polypeptide of claim 1; b) inserting a nucleic acid sequence encoding a selectable marker into the site of the mutation; c) introducing the mutated espA polynucleotide of step b) into a chromosomal espA gene of an organism to produce a mutation in the chromosomal espA gene; and d) selecting organisms having the mutation.
30. The method of claim 29, wherein the nucleic acid sequence encoding a selectable marker encodes resistance to kanamycin.
31. The method of claim 29, wherein the organism is *E. coli*.
32. An organism with a mutated espA gene produced by the method of claim 29.
33. A kit useful for the detection of a EspA polypeptide of claim 1, comprising carrier means being compartmentalized to receive in close confinement therein one or more containers comprising a container containing an antibody which binds to EspA polypeptide.
34. The kit of claim 33, wherein the antibody is detectably labeled.
35. The kit of claim 34, wherein the label is selected from the group consisting of radioisotope, a bioluminescent compound, a chemiluminescent compound, a fluorescent compound, a metal chelate, and an enzyme.
36. A kit useful for the detection of an espA polynucleotide of claim 2, comprising carrier means being compartmentalized to receive in close confinement therein one or more containers comprising a container containing the nucleic acid probe that hybridizes to espA polynucleotide.
37. The kit of claim 36, wherein the probe is detectably labeled.
38. The kit of claim 37, wherein the label is selected from the group consisting of radioisotope, a bioluminescent compound, a chemiluminescent compound, a fluorescent compound, a metal chelate, and an enzyme.
39. A method of producing a fusion protein comprising: a) growing a host cell containing a polynucleotide of claim 2 operably linked to a polynucleotide encoding a polypeptide or peptide of interest under conditions which allow expression and secretion of the fusion protein; and b) isolating the fusion protein.

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1. [20030166841](#). 24 Jan 01. 04 Sep 03. ESCHERICHIA COLI SECRETED PROTEIN B. Kaper, James B., et al. 530/350; C12P019/12 C07K001/00 C07K014/00 C07K017/00.
2. [20030143558](#). 28 May 02. 31 Jul 03. Methods for attenuation of virulence in bacteria. Mitchell, Wayne, et al. 435/6; 702/20 C12Q001/68 G06F019/00 G01N033/48 G01N033/50.
3. [20020160020](#). 03 Jan 02. 31 Oct 02. Enterohemorrhagic escherichia coli vaccine. Finlay, Brett, et al. 424/257.1; 435/252.33 A61K039/108 C12N001/20.
4. [20020115829](#). 28 Sep 01. 22 Aug 02. Pathogenic escherichia coli associated protein. Finlay, B. Brett, et al. 530/350; A61K039/02 C07K001/00 C07K014/00 C07K017/00.
5. [6635259](#). 24 Jan 01; 21 Oct 03. Escherichia coli secreted protein B. Kaper; James B., et al. 424/241.1; 424/185.1 424/190.1 435/6 435/7.1 435/7.2 435/7.32 435/7.37 530/350 530/402. A61K039/08.
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7. [6291435](#). 01 Mar 00; 18 Sep 01. Treatment of diarrhea caused by enteropathogenic Escherichia coli. Yanmaele; Rosa P., et al. 514/25; 514/53 514/867 536/17.2 536/55.1 536/55.2. A61K031/70.
8. [6204004](#). 21 Mar 97; 20 Mar 01. Immunodiagnostic test for enterohemorrhagic Escherichia coli infection. Kaper; James B., et al. 435/7.37; 435/6 435/7.32 530/402 536/23.1. G01N033/569.
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10. [US20030166841A](#). New purified protein called EspB or EspA isolated from enterohemorrhagic Escherichia coli (EHEC), useful for diagnosing whether a subject has been infected with EHEC. JARVIS, K, et al. A61K039/08 C07K001/00 C07K014/00 C07K017/00 C12P019/12.

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-
11. WO 200253181A. Vaccine composition useful for eliciting immunological response in ruminant and for reducing colonization or shedding of enterohemorrhagic Escherichia coli, comprises enterohemorrhagic E. coli cell culture supernatant. FINLAY, B, et al. A61K039/108 A61K039/39 A61P031/04 C07K001/02 C07K001/34 C07K014/245 C12N001/20.
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12. US 6204004B. Diagnosis of active infection by enterohemorrhagic Escherichia coli comprises detecting antibodies to E. coli secreted protein EspA or EspB. JARVIS, K, et al. G01N033/569.
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13. WO 9924576A. New translocated intimin receptor useful for treating infection by enteropathogenic or enterohemorrhagic Escherichia coli. DEVINNEY, R, et al. A61K038/00 A61K038/16 A61P001/00 A61P031/04 C07K014/24 C07K016/12 C12N005/10 C12N015/09 C12N015/31 C12N015/62 C12P021/02 C12P021/08 C12Q001/68 G01N033/53 C12P021/02 C12R001:19.
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L3: Entry 11 of 13

File: DWPI

Oct 8, 2003

DERWENT-ACC-NO: 2002-557723

DERWENT-WEEK: 200370

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TITLE: Vaccine composition useful for eliciting immunological response in ruminant and for reducing colonization or shedding of enterohemorrhagic Escherichia coli, comprises enterohemorrhagic E. coli cell culture supernatant

INVENTOR: FINLAY, B; POTTER, A A

PRIORITY-DATA: 2001US-259818P (January 4, 2001), 2002US-0039760 (January 3, 2002)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
<input type="checkbox"/> EP 1349570 A1	October 8, 2003	E	000	A61K039/108
<input type="checkbox"/> WO 200253181 A1	July 11, 2002	E	053	A61K039/108
<input type="checkbox"/> US 20020160020 A1	October 31, 2002		000	A61K039/108

INT-CL (IPC): A61 K 39/108; A61 K 39/39; A61 P 31/04; C07 K 1/02; C07 K 1/34; C07 K 14/245; C12 N 1/20

ABSTRACTED-PUB-NO: WO 200253181A

BASIC-ABSTRACT:

NOVELTY - A vaccine composition (I) comprises an enterohemorrhagic Escherichia coli (EHEC) cell culture supernatant (CCS) and an immunological adjuvant.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for use of EHEC cell culture supernatant in the manufacture of a composition for eliciting an immunological response in a mammal against a secreted EHEC antigen.

ACTIVITY - Antibacterial; immunostimulant.

MECHANISM OF ACTION - Vaccine; Stimulator of immune response (claimed).

The effect of vaccine containing EHEC CCS on dairy cows were studied. Twenty adult dairy cows were divided in 2 groups of 10 cows. Group 1 was immunized with CCS vaccine and group 2 was immunized with saline-vaccine on days 1 and 22. Seroconversion was assayed by enzyme linked immunosorbent assay (ELISA) on days 1 (pre-immunization), 22 and 36. On days 22 and 36, group 1 cows showed specific antibody titers against EspA and Tir, and group 2 cows showed no specific antibody titers. At day 36, groups 1 and 2 cows were challenged with 108 colony forming units (CFU) of EHEC O157:H7 and shedding was monitored daily for 14 days. Fewer group 1 cows shed EHEC O157:H7 for short period of time than groups 2 cows. After 6 months, group 1 and 2 cows were again immunized. On day 14 following the 2nd boost, antibody titers were assayed by ELISA. Group 1 cows had specific antibody titers to

EspA and Tir, and group 2 cows had no specific antibody titers. On day 14 following the 2nd boost, group 1 and 2 cows were again challenged with 108 CFU of EHEC O157:H7 and shedding was monitored daily for 14 days. Fewer group 1 (CCS) cows shed EHEC O157:H7 for short period of time, than group 2 (saline) cows.

USE - (I) is useful for eliciting an immunological response in a mammal, especially ruminant (bovine subject) against a secreted EHEC antigen, and for reducing colonization or shedding of EHEC (claimed), such as reducing the number of animals shedding EHEC, and reducing the time in which EHEC are shed into the environment, thus reducing the contamination of environment, meat or water. (I) is useful as an adjunct to other biological, chemical, biologically engineered, nucleic acid-based or recombinant protein anti-EHEC agents. (I) is also useful for treating or preventing EHEC infections in other mammals such as humans.

ADVANTAGE - (I) comprising CCS is prepared in an easier and inexpensive manner. CCS is effective at dose regimens that have minimal toxicity.

ABSTRACTED-PUB-NO: WO 200253181A

EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/9

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L3: Entry 11 of 13

File: DWPI

Oct 8, 2003

DERWENT-ACC-NO: 2002-557723

DERWENT-WEEK: 200370

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TITLE: Vaccine composition useful for eliciting immunological response in ruminant and for reducing colonization or shedding of enterohemorrhagic Escherichia coli, comprises enterohemorrhagic E. coli cell culture supernatant

INVENTOR: FINLAY, B; POTTER, A A

PATENT-ASSIGNEE: UNIV BRITISH COLUMBIA (UYBRN), UNIV SASKATCHEWAN (UYSAN), FINLAY B (FINLI), POTTER A A (POTTI)

PRIORITY-DATA: 2001US-259818P (January 4, 2001), 2002US-0039760 (January 3, 2002)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
<input type="checkbox"/> EP 1349570 A1	October 8, 2003	E	000	A61K039/108
<input type="checkbox"/> WO 200253181 A1	July 11, 2002	E	053	A61K039/108
<input type="checkbox"/> US 20020160020 A1	October 31, 2002		000	A61K039/108

DESIGNATED-STATES: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
EP 1349570A1	January 3, 2002	2002EP-0726978	
EP 1349570A1	January 3, 2002	2002WO-CA00019	
EP 1349570A1		WO 200253181	Based on
WO 200253181A1	January 3, 2002	2002WO-CA00019	
US20020160020A1	January 4, 2001	2001US-259818P	Provisional
US20020160020A1	January 3, 2002	2002US-0039760	

INT-CL (IPC): A61 K 39/108; A61 K 39/39; A61 P 31/04; C07 K 1/02; C07 K 1/34; C07 K 14/245; C12 N 1/20

ABSTRACTED-PUB-NO: WO 200253181A

BASIC-ABSTRACT:

NOVELTY - A vaccine composition (I) comprises an enterohemorrhagic *Escherichia coli* (EHEC) cell culture supernatant (CCS) and an immunological adjuvant.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for use of EHEC cell culture supernatant in the manufacture of a composition for eliciting an immunological response in a mammal against a secreted EHEC antigen.

ACTIVITY - Antibacterial; immunostimulant.

MECHANISM OF ACTION - Vaccine; Stimulator of immune response (claimed).

The effect of vaccine containing EHEC CCS on dairy cows were studied. Twenty adult dairy cows were divided in 2 groups of 10 cows. Group 1 was immunized with CCS vaccine and group 2 was immunized with saline-vaccine on days 1 and 22.

Seroconversion was assayed by enzyme linked immunosorbent assay (ELISA) on days 1 (pre-immunization), 22 and 36. On days 22 and 36, group 1 cows showed specific antibody titers against EspA and Tir, and group 2 cows showed no specific antibody titers. At day 36, groups 1 and 2 cows were challenged with 108 colony forming units (CFU) of EHEC O157:H7 and shedding was monitored daily for 14 days. Fewer group 1 cows shed EHEC O157:H7 for short period of time than groups 2 cows. After 6 months, group 1 and 2 cows were again immunized. On day 14 following the 2nd boost, antibody titers were assayed by ELISA. Group 1 cows had specific antibody titers to EspA and Tir, and group 2 cows had no specific antibody titers. On day 14 following the 2nd boost, group 1 and 2 cows were again challenged with 108 CFU of EHEC O157:H7 and shedding was monitored daily for 14 days. Fewer group 1 (CCS) cows shed EHEC O157:H7 for short period of time, than group 2 (saline) cows.

USE - (I) is useful for eliciting an immunological response in a mammal, especially ruminant (bovine subject) against a secreted EHEC antigen, and for reducing colonization or shedding of EHEC (claimed), such as reducing the number of animals shedding EHEC, and reducing the time in which EHEC are shed into the environment, thus reducing the contamination of environment, meat or water. (I) is useful as an adjunct to other biological, chemical, biologically engineered, nucleic acid-based or recombinant protein anti-EHEC agents. (I) is also useful for treating or preventing EHEC infections in other mammals such as humans.

ADVANTAGE - (I) comprising CCS is prepared in an easier and inexpensive manner. CCS is effective at dose regimens that have minimal toxicity.

ABSTRACTED-PUB-NO: WO 200253181A

EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/9

DERWENT-CLASS: B04 C06 D16

CPI-CODES: B04-B04C; B04-F10A3; B10-A22; B14-A01A3; B14-G01; B14-S11B; B14-S12; C04-B04C; C04-F10A3; C10-A22; C14-A01A3; C14-G01; C14-S11B; C14-S12; D05-H07; D05-H08;

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5. Document ID: EP 1349570 A1, WO 200253181 A1, US 20020160020 A1

L6: Entry 5 of 5

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Oct 8, 2003

DERWENT-ACC-NO: 2002-557723

DERWENT-WEEK: 200370

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TITLE: Vaccine composition useful for eliciting immunological response in ruminant and for reducing colonization or shedding of enterohemorrhagic Escherichia coli, comprises enterohemorrhagic E. coli cell culture supernatant

INVENTOR: FINLAY, B; POTTER, A A

PRIORITY-DATA: 2001US-259818P (January 4, 2001), 2002US-0039760 (January 3, 2002)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
<u>EP 1349570 A1</u>	October 8, 2003	E	000	A61K039/108
<u>WO 200253181 A1</u>	July 11, 2002	E	053	A61K039/108
<u>US 20020160020 A1</u>	October 31, 2002		000	A61K039/108

INT-CL (IPC): A61 K 39/108; A61 K 39/39; A61 P 31/04; C07 K 1/02; C07 K 1/34; C07 K 14/245; C12 N 1/20

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L6: Entry 5 of 5

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<input type="checkbox"/> <u>EP 1349570 A1</u>	October 8, 2003	E	000	A61K039/108
<input type="checkbox"/> <u>WO 200253181 A1</u>	July 11, 2002	E	053	A61K039/108
<input type="checkbox"/> <u>US 20020160020 A1</u>	October 31, 2002		000	A61K039/108

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EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg. 0/9

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2. 20030092684. 03 Jan 02. 15 May 03. Compositions and methods for treating hemorrhagic virus infections and other disorders. Fredeking, Terry M., et al. 514/152; A61K031/65.
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3. 20020160020. 03 Jan 02. 31 Oct 02. Enterohemorrhagic escherichia coli vaccine. Finlay, Brett, et al. 424/257.1; 435/252.33 A61K039/108 C12N001/20.
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5. WO 200253181A. Vaccine composition useful for eliciting immunological response in ruminant and for reducing colonization or shedding of enterohemorrhagic Escherichia coli, comprises enterohemorrhagic E. coli cell culture supernatant. FINLAY, B, et al. A61K039/108 A61K039/39 A61P031/04 C07K001/02 C07K001/34 C07K014/245 C12N001/20.
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